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OPY 1

# MEDICAL ANNALS of the DISTRICT OF COLUMBIA

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*July 1967* Vol. XXXVI · No. 7

**Changing Concepts in Chest Fluoroscopy**
Bela Gondos, M.D.

**Rehabilitation of Hard-of-Hearing and Deaf Persons**
Alfred G. Constam, M.S.E.E.

**Allergy to Insect Stings**
Solomon E. Barr, M.D.

**L-8-VP Nasal Spray for Diabetes in Children**
Wellington Hung, M.D.

**Study of Digitalis Toxicity in Large Hospital**
A. A. Tawakkol, M.D., D. O. Nutter, M.D., and R. A. Massumi, M.D.

*(Complete Index on page 5)*

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# MEDICAL ANNALS

## of the District of Columbia

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Hydroxyzine has demonstrated its clinical effectiveness in the chemotherapeutic aspect of the total management of neuroses and emotional disturbances manifested by anxiety, tension, agitation, apprehension or confusion.

**Indications:** Total management in conditions of emotional stress requires in most instances a combined approach of psychotherapy and chemotherapy. Hydroxyzine has been found to be particularly useful for this latter phase of therapy in its ability to render the disturbed patient more approachable and amenable to psychotherapy in long-term treatment of the psychoneurotic and the psychotic, although it should not be used as the sole treatment of psychosis or of clearly demonstrated cases of depression.

Hydroxyzine is also useful in alleviating the manifestations of anxiety and tension in situations in which the causative stress is temporary, as in the preparation for dental and other minor surgical procedures, and in acute emotional problems. It has also been recommended for the management of anxiety associated with organic disturbances such as certain types of heart disease, digestive disorders, dermatoses, senility, the menopausal syndrome, and behavior problems in brain-damaged or epileptic children.

In addition, it has been recommended as adjunctive therapy in alcoholism, and allergic conditions with strong emotional overlay, as in asthma, chronic urticaria, and pruritus.

Hydroxyzine has also demonstrated effectiveness in controlling nausea and vomiting associated with gastritis, gastroenteritis and enteritis; upper respiratory infections, influenza and pneumonia; postoperative conditions; miscellaneous diseases such as Ménière's syndrome, migraine, and vestibulitis.

Hydroxyzine for intramuscular use is especially useful in treating the acutely disturbed or hysterical patient and the acute or chronic alcoholic patient with anxiety withdrawal symptoms or delirium tremens. Used adjunctively pre- and postoperatively and pre- and postpartum, hydroxyzine allays anxiety, permits substantial reduction in narcotic dosage and controls emesis.

Clinical use of hydroxyzine as an adjunct to the management of labor has been extensively reported in the literature without evidence of harm to the mother or fetus.

**Contraindications:** Hydroxyzine, when administered to the pregnant mouse, rat, and rabbit induced fetal abnormalities in the rat at doses substantially above the human therapeutic range. Clinical data in human beings are inadequate to establish safety in early pregnancy. Until such data are available, hydroxyzine is contraindicated in early pregnancy.

Hydroxyzine is contraindicated in any individual who has shown a previous hypersensitivity to it. The parenteral solution is intended only for intramuscular or intravenous administration and should not, under any circumstances, be injected subcutaneously or intra-arterially.

**Precautions:** Drowsiness may occur with oral or parenteral use of this drug , and patients should therefore be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Since hydroxyzine may potentiate the action of central nervous system depressants, conjunctive use with these drugs requires that their dosage be decreased. Hydroxyzine reduces the requirements by as much as 50% for narcotics such as meperidine, so their use in preanesthetic adjunctive therapy should be modified on an individual basis.

As with any preparation for intramuscular injection, Vistaril (hydroxyzine hydrochloride) Parenteral Solution should be injected well within the body of a relatively large muscle such as in the upper outer quadrant of the buttock or the lateral thigh. To avoid the possibility of radial nerve injury, injections should not be made into the lower and middle thirds of the upper arm. Aspiration and proper anatomical selection of injection site should be observed as a precaution against inadvertent injection into a blood vessel or major nerve. In a few instances of reported intravenous administration of hydroxyzine hydrochloride, digital gangrene has occurred distal to the injection site, apparently the result of endarteritis and thrombosis. This event has been considered due to inadvertent intra-arterial injection, although the possibility of periarterial extravasation, with arterial spasm, cannot be ruled out. Therefore, particular caution should be observed when hydroxyzine parenteral solution is administered intravenously to insure that it is injected only into intact veins; avoid either intra-arterial injection or extravasation. Due to infrequent phlebitis resulting from too rapid intravenous administration of the solution, the rate of injection should not exceed 25 mg. per minute. A single intravenous administration in excess of 100 mg. is not recommended (see Adverse Reactions).

**Adverse Reactions:** No serious side effects have been reported and confirmed in the administration of hydroxyzine to date. While therapeutic doses of hydroxyzine seldom produce impairment of mental alertness, transient drowsiness may occur; this may disappear in a few days of continued therapy or upon dosage reduction. Dryness of the mouth may be seen with higher doses. Involuntary motor activity, including rare instances of tremor and convulsions, has been reported, usually with doses considerably higher than those recommended. Extensive clinical use has substantiated the absence of toxic effects on the bone marrow or liver when hydroxyzine was administered in recommended doses for over four years of uninterrupted therapy.

When this product is given intravenously undiluted, minimal amounts of intravascular hemolysis occur at the site of injection. Giving the maximum recommended intravenous dose (100 mg.) to adults results in immediate transient hemolysis with the liberation of a total of 2-3 grams of hemoglobin, which, in some individuals, can cause small amounts of hemoglobinuria. (In the course of normal red cell destruction in the body, approximately 8 Gm. of hemoglobin are liberated every 24 hours.) Therefore, it is recommended that, when given intravenously, parenteral hy-

*(Continued on succeeding page.)*

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HYDROXYZINE PAMOATE

*(Continued from preceding page.)*

droxyzine be diluted with 50 cc. of normal saline and given during a period of four minutes or more; with this technique, drug-induced hemolysis is unlikely.

Dosage: *Oral*—Adults: Dosage varies with individual requirements and ranges from 25 mg. t.i.d. to 100 mg. q.i.d.

Children: *under 6 years,* 50 mg. daily in divided doses; *over 6 years,* 50-100 mg. daily in divided doses.

*Parenteral*—For adult psychiatric and emotional emergencies, including acute alcoholism—I.M.: 50-100 mg. Stat., and q. 4-6 h., p.r.n.; I.V.: 50 mg. Stat., maintain with 25-50 mg. I.V. q. 4-6 h., p.r.n.

Nausea and vomiting—Adults: 25-100 mg. I.M. or I.V.; Children: 0.5 mg./lb. body weight I.M.

Pre- and postoperative adjunctive medication—Adults: 25-100 mg. I.M. or I.V.; Children: 0.5 mg./lb. body weight I.M.

Pre- and postpartum adjunctive therapy—25-100 mg. I.M. or I.V.

Patients may be started on parenteral therapy when indicated by the clinical situation. They should be maintained on oral therapy whenever this route is again practicable.

As with all potent medications, the dosage should be adjusted according to the patient's response to therapy.

Supply: *Vistaril (hydroxyzine pamoate) Capsules*—25 mg., two-tone green capsules; 50 mg., green-and-white capsules; and 100 mg., green-and-gray capsules; in bottles of 100 and 500. Each capsule contains hydroxyzine pamoate equivalent to 25 mg., 50 mg., or 100 mg. of hydroxyzine HCl.

*Vistaril (hydroxyzine pamoate) Oral Suspension*—Equivalent to 25 mg. hydroxyzine HCl per 5 cc. teaspoonful, in 1 pint bottles.

*Vistaril (hydroxyzine HCl) Parenteral Solution*—10 cc. vials, 25 and 50 mg. per cc.; 2 cc. vials, 50 mg. per cc., in packages of 6 vials; Isoject,® 25 and 50 mg. per cc., 1 cc. per unit. Isoject, 100 mg. per 2 cc. unit, 50 mg. per cc.

Composition (Parenteral Solution)

| Each cc. contains: | 25 mg./cc. | 50 mg./cc. |
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| Hydroxyzine hydrochloride | 25 mg. | 50 mg. |
| Benzyl alcohol | 0.9% | 0.9% |
| Sodium hydroxide (approx.) to adjust to optimum pH | 0.22% | 0.46% |
| Water for Injection | q.s. | q.s. |

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## NATIONAL AND REGIONAL MEETINGS

August 7–10: National Medical Association. Chase Park Plaza, St. Louis. Address: Mr. Samuel C. Smith, Administrative Secretary, 520 W Street, N.W., Washington, D. C. 20001.

August 11–13: International Doctors in Alcoholics Anonymous. Airlie, Warrenton, Va. Address: Dr. Earl H. Mitchell, 3509 Dunlop Street, Chevy Chase, Md. 20015.

**August 23–26: American Physiological Society. Howard University, Washington. Address: Dr. Ray G. Daggs, Executive Secretary, 9650 Rockville Pike, Bethesda, Md. 20014.**

**August 27–31: American Society for Pharmacology and Experimental Therapeutics. Howard University, Washington. Dr. Ellsworth B. Cook, Executive Secretary, 9650 Rockville Pike, Bethesda, Md. 20014.**

August 27–September 1: American Academy of Physical Medicine and Rehabilitation. Americana Hotel, Miami Beach, Fla. Address: Mr. Creston C. Herold, Executive Director, 30 North Michigan Avenue, Chicago, Ill. 60602.

**September 1–3: Society for Clinical and Experimental Hypnosis. Washington. Dr. Ericka Fromm, Executive Secretary, 5843 University, Chicago, Ill. 60637.**

September 7–9: American Association of Obstetricians and Gynecologists. The Homestead, Hot Springs, Va. Address: Dr. Robert B. Wilson, Secretary, 200 First Street, S.W., Rochester, Minn.

September 10–15: Flying Physicians Association. Williamsburg Inn, Williamsburg, Va. Address: Mr. Albert Carriere, 332 South Michigan Avenue, Chicago, Ill. 60614.

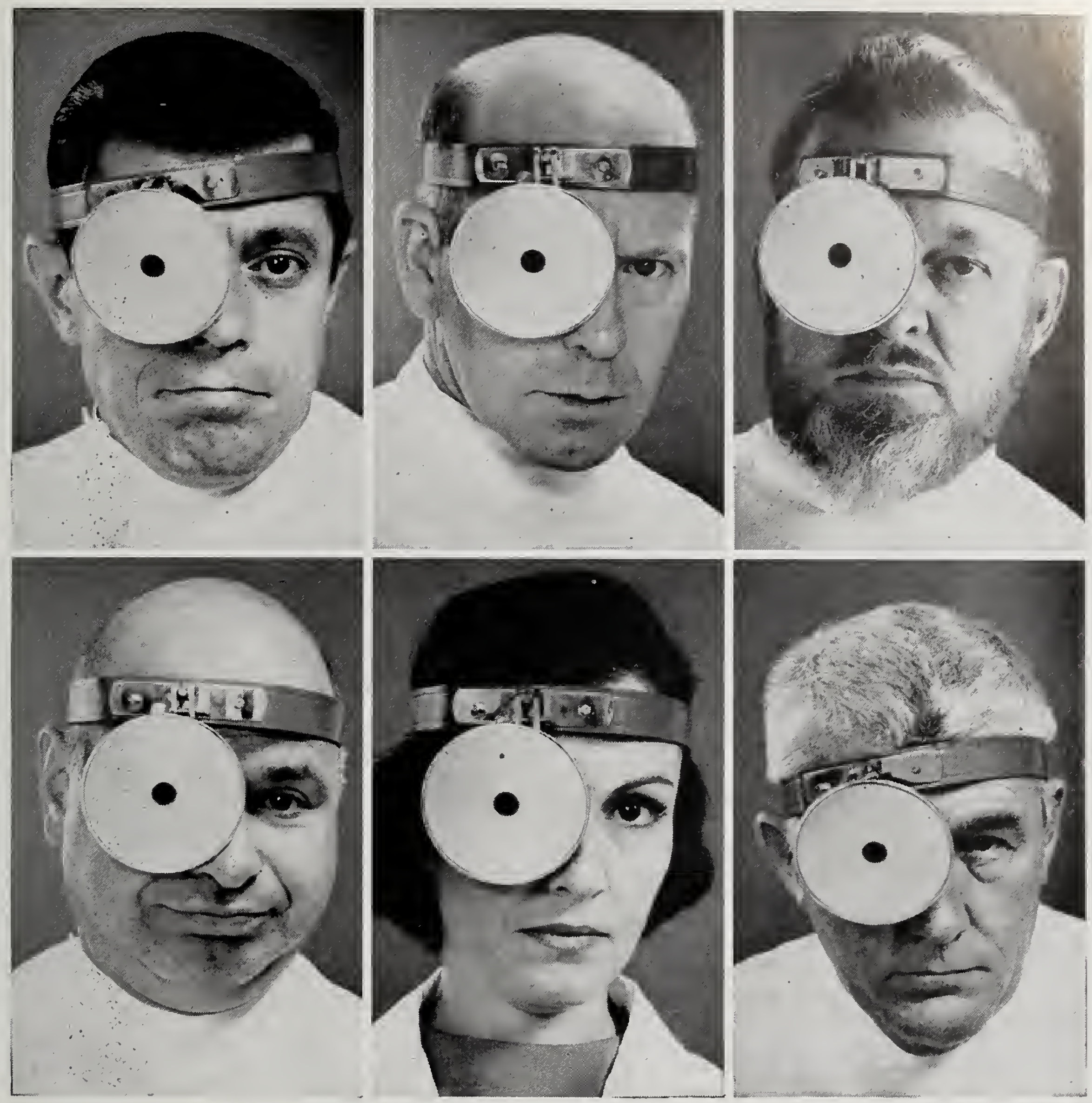
September 15–16: Tidewater Heart Association (8th Annual Cardiovascular Symposium). Golden Triangle Motor Hotel, Norfolk, Va. Address: Dr. Robert J. Robertson, Chairman, 523 Boush Street, Norfolk, Va. 23510.

September 18–21: American Academy of General Practice. Market Hall, Dallas. Address: Mr. Mac F. Cahal, Executive Director, Volker Blvd. at Brookside, Kansas City, Mo. 64112.

**September 25: Society for Pediatric Radiology. Washington Hilton Hotel, Washington. Address: Dr. John L. Gwinn, Secretary-Treasurer, Children's Hospital, 4614 Sunset Blvd., Los Angeles, Calif. 90027.**

**September 26–29: American Roentgen Ray Society. Washington Hilton Hotel, Washington. Address: Dr. Ted F. Leigh, Secretary, Emory University Clinic, Atlanta, Ga. 30322.**

**November 20–22: Annual Scientific Assembly, The Medical Society of the District of Columbia. Statler-Hilton Hotel, Washington. Address: Mr. George W. Cooley, Executive Director, 2007 Eye Street, N.W., Washington, D. C. 20006.**



# "All Otolaryngologists are Alike"

Just look at them and you can see how much they have in common. Besides, they all go through pretty much the same training, and pass the same kinds of tests, and measure up to the same sort of standards. Therefore, all otolaryngologists are alike. Right?

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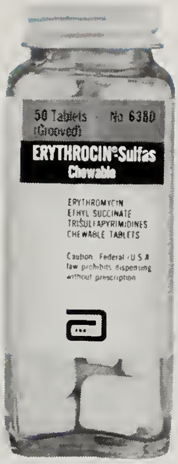
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(Erythromycin ethyl succinate-trisulfapyrimidines granules for oral suspension)

87 patients were treated[1,2]—all children, ages four months to 15 years.

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53 were clinically cured within 72 hours, while 32 showed partial relief within the same time, and subsequent clinical cure.

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Brief Summary on next page

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1. Case Reports on File, Dept. Clin. Development, Abbott Laboratories.
2. Polley, R.F.L., Use of Erythromycin-Sulfas in Office Practice, Western Med., 7:177, July, 1966.

**ERYTHROCIN®-SULFAS**
Brief Summary

**Contraindications:** Known sensitivity to erythromycin or sulfonamides. Because of the possibility of kernicterus with sulfonamides, do not use in pregnancy at term, premature or newborn infants.

**Warnings:** As with other forms of sulfonamide therapy, carefully evaluate patients with liver or kidney damage, urinary obstruction, or blood dyscrasia. Deaths have been reported from hypersensitivity reactions and blood dyscrasias following use of sulfonamides. Perform blood counts and liver and kidney function tests if used repeatedly at close intervals or for long periods.

**Precautions, Side Effects:** Occasionally mild abdominal discomfort, nausea or vomiting may occur with erythromycin, generally controlled by reduction of dosage. Mild allergic reactions (such as urticaria and other skin rashes) may occur. Serious allergic reactions have been extremely infrequent. Use sulfonamides with caution in patients with a history of allergy. Assure adequate fluid intake to prevent crystalluria and institute alkali therapy if indicated. If overgrowth of nonsusceptible organisms occurs, withdraw the drug and institute appropriate treatment. If a patient should show signs of hypersensitivity, appropriate countermeasures (e.g. epinephrine, steriods, etc.) should be administered and the drug withdrawn.

**Adverse Reactions:** Sulfonamide therapy may be associated with headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.

Side effects due to erythromycin are infrequent, but occasional abdominal discomfort, nausea, or vomiting, urticaria and other skin rashes may occur.

**Supplied:** The Granules for Oral Suspension come in bottles of 60 ml. and 150 ml. The Chewable tablets are in bottles of 50. Each 5-ml. teaspoonful of reconstituted Granules or each Chewable tablet provides erythromycin ethyl succinate equivalent to 125 mg. of erythromycin activity and 167 mg. of each of sulfadiazine, sulfamerazine and sulfamethazine.

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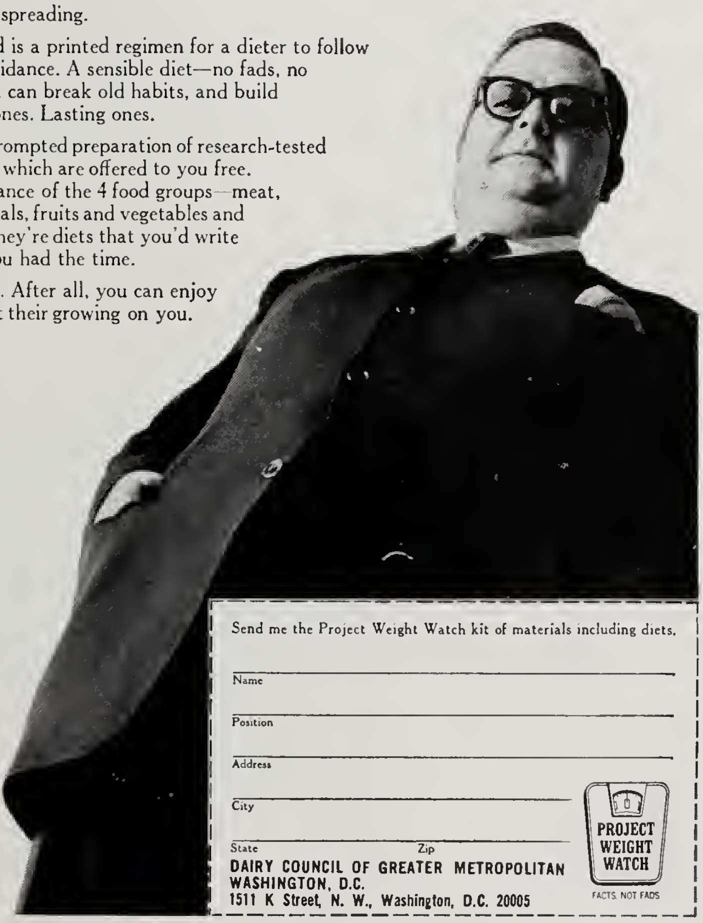

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*Precautions:* Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage. Make regular blood counts. Discontinue the drug and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

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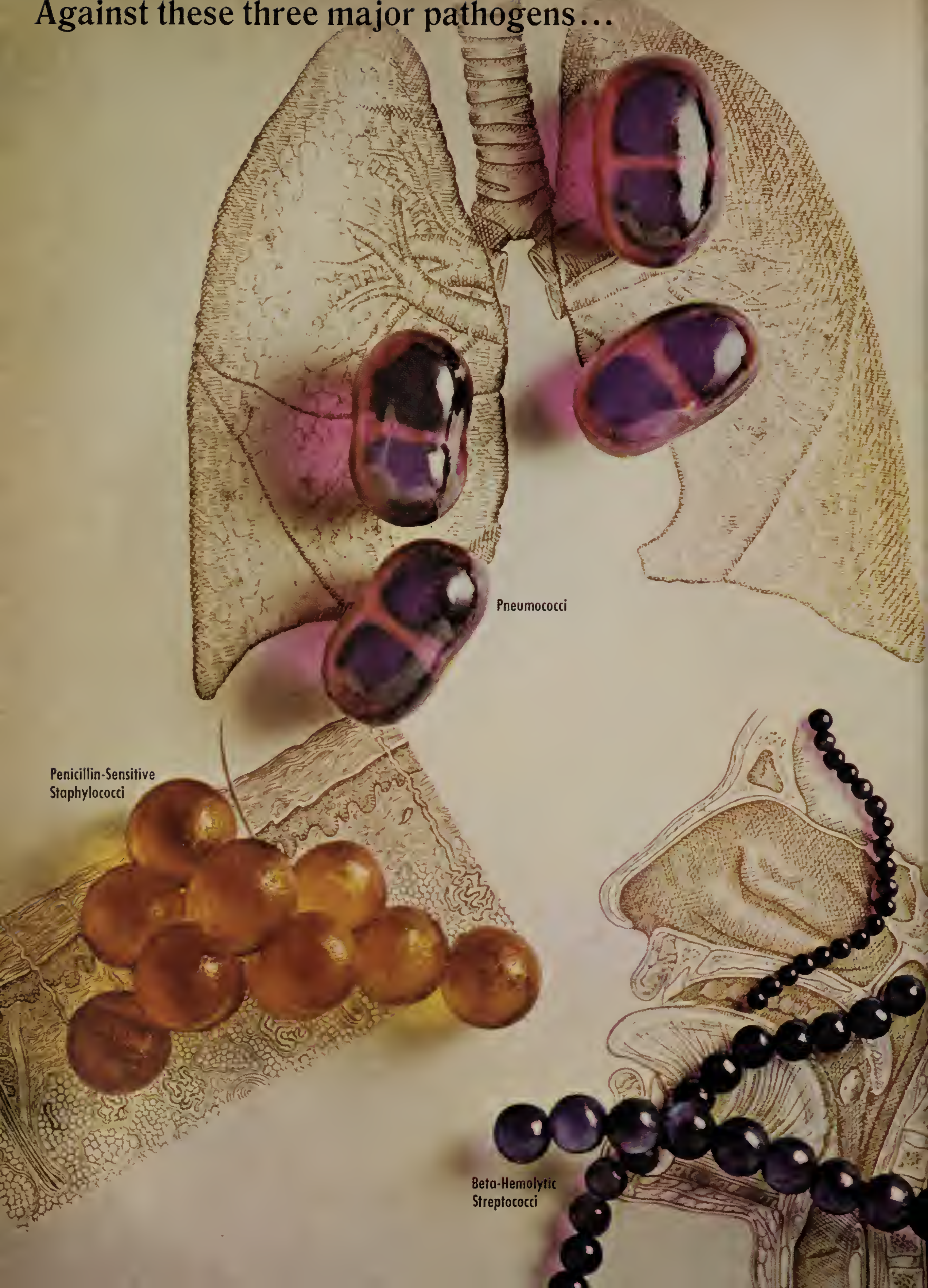
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| Penicillin G | 0.02 | 0.005-1.6 | 0.005 | 0.002-0.2 | 0.02 | 0.01-0.1 |
| Methicillin | 1.6 | 0.4-6.3 | 0.2 | 0.1-0.4 | 0.2 | 0.1-1.6 |
| Oxacillin | 0.4 | 0.1-3.1 | 0.04 | 0.02-0.4 | 0.1 | 0.04-0.8 |
| Cloxacillin | 0.2 | 0.2-0.8 | 0.1 | 0.1-0.8 | — | — |
| Nafcillin | 0.4 | 0.2-0.8 | 0.04 | 0.02-0.1 | 0.02 | 0.02-0.2 |
| Ampicillin | 0.2 | 0.1-0.8 | 0.02 | 0.01-0.04 | 0.02 | 0.01-0.04 |

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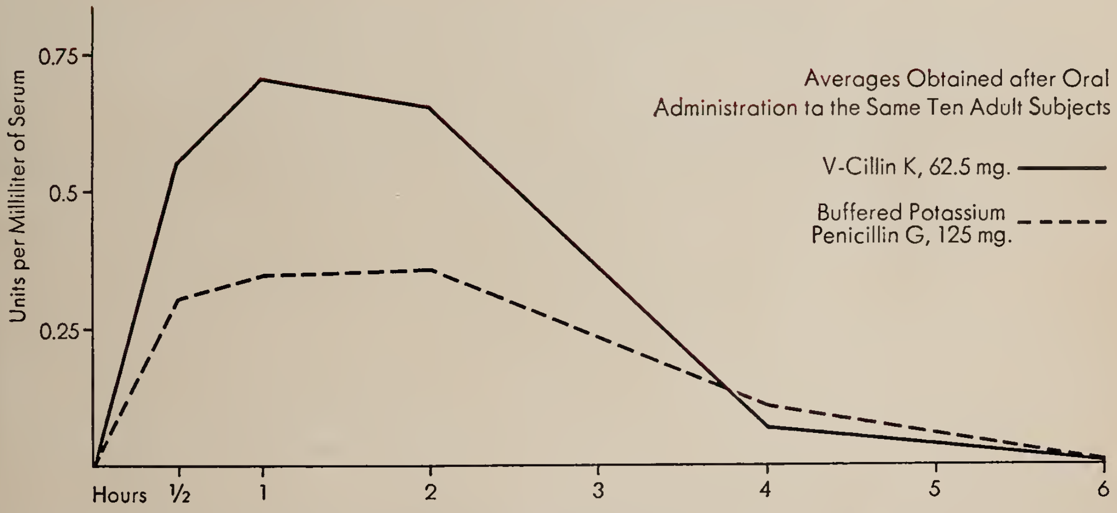

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V-Cillin K, Pediatric, is an oral solution of clinically proved V-Cillin K in teaspoon dosage form. When mixed as directed, each 5 cc. (approximately one teaspoonful) will contain 125 mg. (200,000 units) phenoxymethyl penicillin as the potassium salt.

**Indications:** V-Cillin K has been shown to be effective in the treatment of streptococcus, pneumococcus, and gonococcus infections as well as infections caused by sensitive strains of staphylococci. It may be used for the prophylaxis of streptococcus infections in patients with a history of rheumatic fever and for the prevention of bacterial endocarditis after tonsillectomy and tooth extraction in those patients with a history of rheumatic fever or congenital heart disease.

**Contraindication:** V-Cillin K should not be administered to a patient with a history of penicillin hypersensitivity.

**Warnings:** In rare instances, the use of penicillin may cause acute anaphylaxis which may prove fatal unless promptly controlled. This type of reaction appears more frequently in patients with a history of sensitivity reactions to penicillin and in those with bronchial asthma or other allergies. Resuscitative drugs should be readily available for emergency administration. These include epinephrine and pressor drugs (as well as oxygen for inhalation) for relief of immediate allergic manifestations and antihistamines and corticosteroids for delayed effects.

**Precautions:** V-Cillin K should be used cautiously, if at all, in a patient with a strongly positive history of allergy.

In prolonged therapy with penicillin, and particularly with hig parenteral dosage schedules, frequent evaluation of the renal an hematopoietic systems is recommended.

In suspected staphylococcus infections, proper laboratory studie (including sensitivity tests) should be performed.

The use of penicillin may be associated with the overgrowth c pencillin-insensitive organisms. In such cases, its administration shoul be discontinued, and appropriate measures should be taken.

**Adverse Reactions:** Although serious allergic reactions are much les common with administration of oral penicillin than with intramuscula forms, manifestations of penicillin allergy may occur.

Penicillin is a substance of low toxicity, but it does possess a significant index of sensitization. The following hypersensitivity reaction associated with the use of penicillin have been reported: skin rashe ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; and reactions resembling serum sickness, including chills, fever edema, arthralgia, and prostration. Severe and often fatal anaphylaxi has occurred (see Warnings). Hemolytic anemia, leukopenia, thrombocytopenia, and nephropathy are rarely observed side-effects anc are usually associated with high parenteral dosage.

**Administration and Dosage:** For Tablets V-Cillin K and for V-Cillin K, Pediatric, the usual dosage ranges from 125 mg. (200,000 units) three times a day to 500 mg. (800,000 units) every four hours. For infants, the daily dosage may be 50 mg. per Kg. of body weight divided into three doses.

Beta-hemolytic streptococcus infections without associated bacteremia may be treated with 200,000 to 400,0000 units three times a day. Therapy should be continued for a minimum of ten days to prevent development of rheumatic fever and/or other serious complications. Dosage for routine streptococcus prophylaxis in patients with a history of rheumatic fever or congenital heart disease may be 200,000 units once or twice daily. When such patients undergo tonsillectomy, tooth extraction, or other minor surgery, the prophylactic dose should be 500,000 units every six hours given two days prior to surgery and for two days postoperatively. If oral medication is not feasible on the day of surgery, parenteral therapy should be considered. Mild to moderately severe pneumococcus pneumonia has been treated effectively with 250 mg. every six hours.

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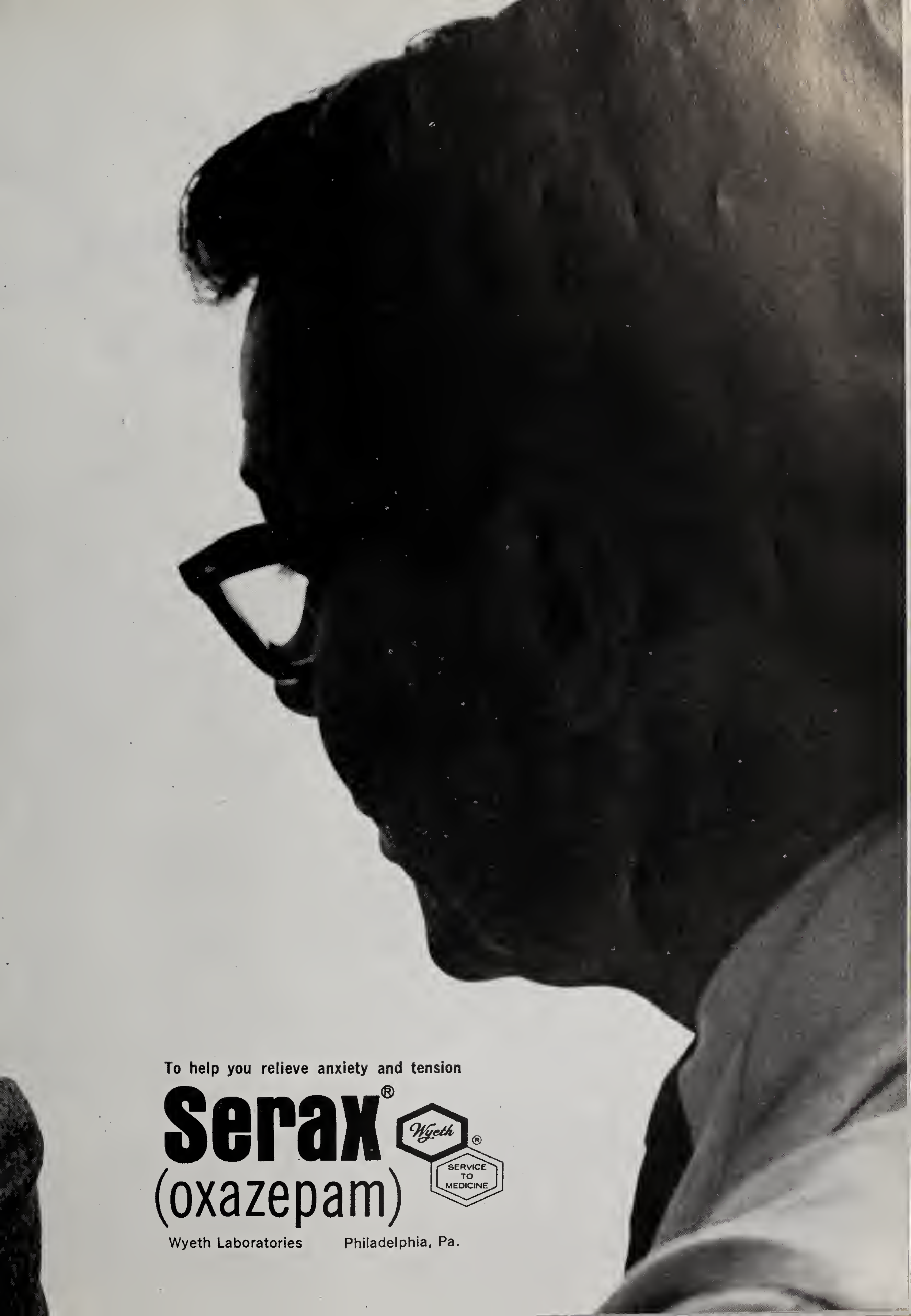

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MEDICAL ANNALS

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*July 1967* VOLUME XXXVI • NUMBER 7

# Changing Concepts in Chest Fluoroscopy

BELA GONDOS, M.D.*

THE ERA when fluoroscopy of the chest was considered an independent diagnostic procedure seems to be over. The school of thought which requires that fluoroscopy be used only as a complementary procedure to roentgenography in chest X-ray examinations and that its indications be limited is increasing in acceptance.[1-4] As the result of this changing concept fluoroscopy and roentgenography cannot be considered as 2 competitive methods but rather as complementary modalities of 1 examination. Nevertheless, chest fluoroscopy is still used as an independent procedure, or if it is combined with roentgenography it is not uncommon that fluoroscopy is the first employed modality. The main reasons of the preference given to fluoroscopy are an inadequate appreciation of the relative value of the 2 methods of examination and a disregard of the requirements based on our increasing knowledge in radiation biology.

## The Relative Value of Fluoroscopy versus Roentgenography in Examination of the Chest

The diagnosis in chest X-ray examination, as generally in physical examination, is approached through 3 phases: The abnormality should be discovered, the details are noted, and the observations evaluated. The discovery of a disease, i.e., a differentiation of the normal from the abnormal, involves an evaluation, and at times this presents more difficulties than the differential diagnosis of a pathologic process. In this review of the comparative value of the 2 methods of X-ray examination an attempt will be made to include all of the 3 phases for evaluation.

In principle, the main indication of fluoroscopy is discovering and observing moving structures and dynamic events. Motion, which generally unfavorably affects roentgenography by blurring the image, represents a most useful feature in fluoroscopy. An evaluation of the diaphragmatic excursion by fluoroscopy in the question of phrenic nerve paralysis, of an infradiaphragmatic abscess, or in a search for pulmonary infarction, etc., is an important part of making an X-ray diagnosis. It should be noted, however, that the position of the diaphragmatic leaflets at the end of the inspiratory and expiratory excursions can usefully be recorded on a roentgenogram if the 2 exposures are made on the same X-ray film. This provides an advantage over fluoroscopy by enabling the examiner to compare the positions of the 2 leaflets in a more exact manner and even to measure the differences in position. This method, limited to the purposes described, can be a good substitute for fluoroscopy (figure 1). Roentgenography, however, cannot replace the "sniff method," which is a more sensitive procedure and should be preserved for fluoroscopy. In this procedure a rapid inspiratory movement through the nose is made. The rapid contraction of the diaphragm is followed by a lag of the normally expanding lung, and this results in an increase of the negative pressure within the respective hemithorax. As a result the difference in the excursion of the 2 leaflets, if a paralysis, paresis or muscular weakness is present, becomes more pronounced. The Valsalva and Müller maneuvers in vascular abnormalities, as in arteriovenous malformations of the lung or possibly in a case of pulmonary varix, by changing the size of the lesion during these procedures as observed on fluoroscopy, are recognized diagnostic methods. In a differential diagnostic problem of a superior mediastinal mass the diagnosis of a retrosternal thyroid can be made by fluoroscopy if the mass moves upward following the positional change of the trachea during the swallowing act or on coughing. The importance of this procedure is emphasized by the fact that a tortuous or widened innominate or subclavian artery may incorrectly be interpreted as a retrosternal thyroid on a frontal roentgenogram. In cardiovascular abnormalities calcification in the left atrial wall in the case of rheumatic heart disease, in the left ventricular wall in cardiac aneurysm, in the coronary artery, of the valves or of the annulus fibrosus, and in cases of small calcification of the pericardium fluoroscopy may provide useful information. Studies of the cardiac and vascular dynamics are also indications for chest fluoroscopy. These include demonstration of paradox (or absence of) pulsation in a left ventricular aneurysm, absence of pulsation of the heart silhouette in pericardial effusion, and increased amplitude of pulsation of the pulmonary arteries in congenital heart diseases connected with left-to-right shunt.

---

* Chief Medical Officer, Radiology Division, District of Columbia General Hospital, Washington, D. C. 20003; Associate Clinical Professor of Radiology, Georgetown University School of Medicine; Assistant Clinical Professor of Radiology, George Washington University School of Medicine and Howard University College of Medicine.

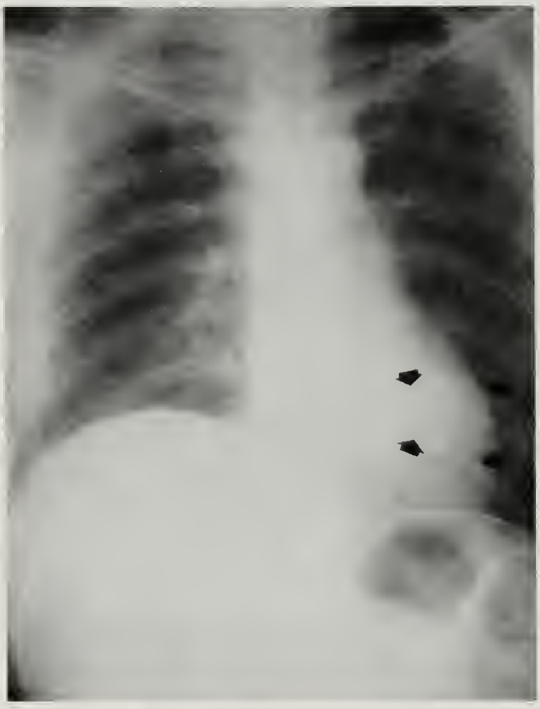

**FIG. 1. Posteroanterior view of chest with 2 exposures (in inspiration and expiration) on the same film. Right hemidiaphragm does not move on respiration, while the left hemidiaphragm makes normal respiratory excursions. (The expiratory position of the left hemidiaphragm is indicated by arrows.) This is a 46-year-old man who had cancer of the middle third of the esophagus and a metastatic tumor mass in the right supraclavicular area. The latter lesion was palpable and produced Horner's syndrome, hoarseness, and right phrenic nerve paralysis demonstrable by fluoroscopy and by this roentgenogram.**

Roentgenography in general is far superior to fluoroscopy in the diagnosis of lung disease. A comparative study[5] on the reliability of fluoroscopy and roentgenography in 200 patients in 1933 revealed a fluoroscopic error, both in a positive and negative sense, in about 50 per cent of the patients examined. In other words, in approximately every second patient fluoroscopy either failed to reveal lesions which were demonstrable on the respective roentgenograms, or, if discovered, the observation regarding details was incorrect.

Small lesions like those in miliary tuberculosis, particularly in the early phases, remain undiagnosed on fluoroscopy, while roentgenography makes an early diagnosis possible. The same applies to small infiltrations, e.g., in the reinfection type of tuberculosis and small malignant lesions. Roentgenography is far superior to fluoroscopy in evaluating important details like the contour of a lesion or a small cavity or calcification within it.

For determination of the size, shape and location of the heart and great vessels roentgenography is generally adequate. Also gross deformities of the cardiovascular structures like aneurysm of the heart or aorta, dilatation of the pulmonary artery and its branches, and enlargement of the left atrium can easily be observed.

In the process of evaluation, roentgenography provides such advantages which, by the very nature of the method, are not present in fluoroscopy:

1. Fluoroscopic procedure is limited in time, while a roentgenogram can be studied indefinitely.
2. Fluoroscopic observation is evaluated and reëvaluated by the virtue of memory, while a roentgenogram is an objective testimony of the examination. This feature is particularly important in follow-up studies, when the examination is to be compared with an old observation.

Electronic amplification of the brightness of the fluoroscopic image, a recently introduced improvement, has considerably increased the possibility of both recognition of small lesions and of observation of finer details. Also, the greatly increased brightness made a decreased dosage of exposure, both for the patient and the examiner, possible. The attachment needed for the image amplification, however, is bulky, and its use is still cumbersome. It is relatively too expensive at present for use by the general physician. Though image amplification has significantly advanced the value of fluoroscopy, many of the inherent deficiencies have remained essentially unchanged. More time and experience will be needed for a more adequate assessment regarding the relative value of this significant technological improvement. The considerations presented in this paper are applied to the conventional method of fluoroscopy without the use of the image amplifier.

### Radiation Hazard in Chest Fluoroscopy

The somatic effects of radiation became known in the pioneer years of diagnostic roentgenology by manifestations of chronic dermatitis, ulcer, and malignancy of the fingers of persons using this newly introduced method of examination. Fluoroscopists of the early years of this discipline commonly used their hands for the evaluation regarding the quality of radiation produced by the respective gas tubes, having no or inadequate knowledge about the biologic effects of radiation. Later observations suggested that carcinoma of the thyroid gland occurs more commonly in children who were given radiation treatment for "thymus enlargement." This treatment has been abandoned since its potential danger is known; also, in contrast to the previous concept, it is now generally recognized that there is no need for X-ray treatment in cases of a larger thymus, because it does not represent any danger to the infant's life.

After the early years of roentgenology it became obvious that radiation may produce not only local damage but generalized affections as well, the hemopoietic system being particularly radiosensitive. Leukemia is believed to be a potential sequence of prolonged radiation exposure in small doses to professional personnel. An increased incidence of leukemia has also been observed in persons who received radiation therapy for ankylosing spondylitis.[6] In animal experiments premature aging and shorter life expectancy were demonstrated.

The genetic effect of radiation produced by primary or scattered radiation to the gonads differs from the "somatic effect" by its potential damage to the health of future generations. There is little doubt that radiation reaching the gonads induces genetic mutation. These mutations are mostly deleterious, and probably there is no threshold dose below which no damage occurs.[7-10] For these reasons and in view of the increasing proportion of the population involved in diagnostic X-ray examinations, radiation damage is no longer a problem of the individual alone. It has been estimated that the number of persons examined by X-rays is constantly increasing at the rate of about 8 per cent a year.[11] Though the individual doses of exposure are usually small, the total dose to the population, and more specifically to the genetic material of the population as a whole, is of increasing concern. Thus, protection against excessive radiation during recent years has become a public health problem.

On the other hand, the occupational hazard of the somatic effect to professional personnel seems gradually decreasing as the result of more awareness of the radiation effects and of the significant advancements in X-ray technology. This is demonstrated in a recent paper[12] which reviewed and compared the mortality statistics of physicians in 3 different specialty groups: members of the Radiological Society of North America, the American College of Physicians, and the American Academy of Ophthalmology and Otolaryngology during 3 calendar periods (1935–1944, 1945–1954, and 1955–1958). As was expected, according to the degree of exposure the mortality rates were the highest among the radiologists, intermediate among the internists, and lowest among the ophthalmologists and otolaryngologists. The figures also indicated a decreasing and almost disappearing difference in the mortality rates of the 3 specialty groups during recent years. This interesting paper not only convincingly documented the existence of the occupational hazard of radiation but also the dramatic effectiveness of measures employed in radiation protection.

It should be kept in mind that in infants and children radiation hazard is greater than in adults if the same diagnostic procedure is employed. By using the usual diaphragmatic aperture in fluoroscopy the dose of exposure in proportion to the body surface and volume is larger than in adults. The effect, in the terms of total body radiation, is the same as the usage of larger fields in adult persons. Also, the growing tissues of children are probably more radiosensitive than those of adults; consequently, a potentiated somatic effect can be expected. Because of the smaller dimensions of the body of an infant or a child, the distance of the gonads from the site of exposure is shorter in chest fluoroscopy (and roentgenography), and their dose of exposure in terms of percentage of the useful radiation is more.[13] Attention should also be given to the fetus in the uterus whenever an X-ray examination of a pregnant woman is considered. The fetus is particularly radiosensitive during the first 3 fetal months, and any abdominal X-ray examination of the mother should be avoided during this period except in true emergencies. It has been suggested that any type of X-ray examination of females in the child-bearing age be limited to the first 9 days following the beginning of the last menstrual period, during which time the existence of an early unrecognized pregnancy is unlikely.[14]

These considerations need more emphasis if fluoroscopy is the modality selected for X-ray examination. In fluoroscopy of the chest the patient's skin is exposed to a dose which is at least 100 times more than that received on the exposure for a frontal chest roentgenogram. According to another calculation made on children the skin dose obtained on a chest film exposure is equivalent to a dose received on fluoroscopy of one-fourth of a second duration.[15]

The above-mentioned calculations were made under favorable circumstances, when the elementary requirements of radiation protection were met and when the fluoroscopist was experienced. Recent surveys show, however, that the majority of registered X-ray units in the United States of America installed in medical offices are in the possession of physicians who have no formal training in diagnostic roentgenology.[16] This was found in the State of California,[17] in the City of New York (in 85 per cent),[18] and in Polk County, Florida (in 94 per cent).[19] It should be considered, however, that the distribution of X-ray equipment does not correctly reflect that of the number of X-ray examinations performed. In the last mentioned survey X-ray examinations were found to be carried out in the majority of instances by physicians other than radiologists, although the respective percentage was smaller than that of the X-ray equipments registered (94 and 70). A recent study undertaken by the U. S. Public Health Service estimates that approximately 28 per cent of medical X-ray procedures were performed without the supervision of a radiologist.[20] Other estimates claim that about half of the fluoroscopic examinations in the United States are conducted by nonradiologists.[2,4] The survey in Polk County, Florida recorded 19 per cent of the fluoroscopies (of any type) performed by nonradiologists.[19]

The conclusion may be made that the majority of X-ray examinations and a considerable proportion of fluoroscopic studies in the United States are carried out by physicians other than radiologists. This is an important observation, because it has been shown that in inexperienced hands the radiation dose to the patient may reach excessive proportions.[21]

It has been stated that the dose to an average person as well as to the whole population delivered by the diagnostic use of X-rays has been far below the dangerous level.[22] Also, it is claimed that there is a threshold dose in the somatic effect below which no permanent damage occurs.[22] The question of threshold effect, however, is still being debated. The latent and subclinical nature of the radiation effect produced by small doses may obscure the existence of such an effect, or, if it is present, a causative relationship with radiation is not easily evident. Threshold dose of radiation, if it exists, should be differentiated from a dose producing "subclinical damage." The present paper follows the thinking of the National Committee of Radiation Protection and Measurement which claims that "unnecessary radiation should always be avoided and all exposures held to a minimum compatible with the practical clinical requirements." Also, it should be kept in mind that the effect of radiation is cumulative. It is unpredictable how much additional radiation an individual or a large segment of the population will have to accept in the future. This consideration applies not only to medical but also to industrial and military applications of radiation sources.

## Fluoroscopy and Radiation Protection

The concept that fluoroscopy is simply "another office procedure" of the practicing physician is false and hazardous. The belief of some that it is sufficient for the examiner merely to know how to push the foot switch and how to handle the shutter is as wrong as to think that the use of a lead apron and gloves is the full answer to the question of radiation protection. The elementary requirements of radiation protection are well publicized, but a reëmphasis here probably will not be a useless repetition. They include the following:

1. Satisfactory structural shielding should be provided and modern X-ray equipment should be used which meet the requirements of Handbook No. 76 of the National Bureau of Standards, published in 1961.[23] This handbook was prepared on the basis of the recommendations of the National Committee of Radiation Protection and Measurements, and its authority is generally accepted.

The requirements for up-to-date X-ray facilities are commonly not met, particularly among nonradiologists. An example is provided by a survey[21] of 35 X-ray installations used by 45 pediatricians (1957) in which only 6 X-ray equipments were found to have a definite limitation of the diaphragmatic opening within the margin of the screen. Also, "on several fluoroscopes the screen and the tube moved independently of each other, a very dangerous feature."

2. Lead gloves and apron should be worn. This requirement is frequently neglected.[21]

3. Adequate dark adaptation is a requirement which is commonly disregarded or incompletely done, resulting in an unsatisfactory examination and prolonged exposure.[21, 24]

4. The field of exposure (the diaphragmatic aperture) should be small.

5. Exposure should be limited to useful observation only.

6. The entire length of fluoroscopic exposure should be limited to a possible minimum. For this purpose a timing device is available on the control panel in modern equipments. This device turns off the apparatus when the total exposure exceeds the predetermined limit.

7. The output of radiation at the tabletop should be calibrated and should not exceed 10 R's per minute. This requirement was not met in a survey[21, 24] except in 12 of the 34 fluoroscopic units.

During recent years it has been increasingly recognized that radiation protection means more than to have good technical facilities and not merely to follow procedural requirements of radiation protection as outlined above. It is believed by many that a more thorough knowledge and training of physicians in the fundamentals of diagnostic roentgenology are an essential part of radiation protection. The chest fluoroscopist should be required to have a basic knowledge in diagnostic roentgenology and in the principles utilized in chest fluoroscopy; he has to be familiar as well with the limitations of these procedures.

Normal roentgen-anatomy is a subject not always adequately appreciated in the teaching of clinical diagnostic roentgenology, particularly at the postgraduate level, if this teaching is not a part of the specialty training in radiology. It is disappointing to find a student of this discipline to have a sophiscated knowledge in the roentgen differential diagnosis of rather uncommon chest diseases but inadequately oriented in roentgen-anatomy of the normal hilus structures. The fluoroscopist who is inadequately oriented in normal roentgen-anatomy and clinical diagnostic roentgenology represents a potential serious offender of the requirements of radiation protection. He may be likened to an automobile driver who wants to locate an address in a city during the evening hours but who is without sufficient knowledge of the respective geography. In a prolonged search he runs around from street to street, and without help he may never find the place. In addition the streets are poorly illuminated, not unlike the dim fluoroscopic image. Experience shows that inadequately trained fluoroscopists use not only longer times of exposure but also larger diaphragmatic openings, the latter being an additional source of increased dose of radiation. With increasing knowledge in roentgen-anatomy and clinical diagnostic roentgenology the students become gradually satisfied with smaller fields for orientation and shorter fluoroscopic time for satisfactory observation.

Fluoroscopy of the chest as an independent examination should be abandoned.[3, 4, 18] Whenever employed, it should always be preceded by roentgenography and used only as a complementary procedure. After a study of the roentgenograms (frontal and lateral), generally the thoracic lesion in question is already located and the questions needed for clarification formulated. The subsequent "aimed" fluoroscopy may require only a limited time of exposure.[2] The application of this approach to the roentgen diagnosis has the same advantage as the automobile driver has who is well oriented in the respective geography and heads immediately in the right direction using the shortest possible way. This requirement is not generally observed as indicated by a survey carried out by the Health Department of the District of Columbia, which revealed that 50 of the 322 medical offices using X-ray equipment, i.e., 15 per cent, were suitable for fluoroscopic examinations only. In Montgomery County, Maryland, the respective proportion was 12 per cent. It is reported that in New York City there are more fluoroscopes than radiographic units registered.[25] According to their design these equipments are generally used for fluoroscopy as an independent procedure only, though occasionally roentgenograms are also taken with them. In a survey of 35 X-ray installations there were only 2 offices where roentgenograms were made.[21] It should also be considered that fluoroscopic examinations as a single and independent procedure are probably done in offices where the apparatus is suitable for both fluoroscopy and roentgenography. Coffey[13] states that "office fluoroscopy is rarely checked with films." A limited and informal survey of mine among physicians other than radiologists revealed that a considerable proportion of fluoroscopic examinations are performed first, even if combined with roentgenography. The correct procedure, of course, is considered the reversal of this order.

It is concluded and suggested that the usage of chest fluoroscopy as generally practiced today needs reconsideration.

### Radiation Protection and Education

Governmental intervention and legislation may be able to usefully control radiation protection in the diagnostic application of X-rays to a limited extent only. Surveys of X-ray equipment by health departments in the United States with voluntary coöperation of the medical profession seem to produce beneficial results in recognizing technical deficiencies and faulty procedures. They also seem to be useful in directing the attention of physicians to the importance of radiation protection. Licensing of X-ray technicians and compulsory examinations prior to licensing are required by law in the State of New York and are under consideration in other states. Such legislation is expected to protect patients from unnecessary and excessive radiation due to inadequate roentgen technique. Expert technique in roentgenography, by the mere fact that it produces the most informative roentgenograms possible, effectively serves the purposes of radiation protection. Inadequate technique by providing unsatisfactory or incorrect information may require additional X-ray studies which otherwise would not be indicated. Ways should also be found to eliminate from the market X-ray equipment usable for fluoroscopy only. This probably can be achieved by the voluntary coöperation of the manufacturers. Such a step is expected to eliminate a part of fluoroscopies performed as independent procedures.

The method of examination to be selected by the physician cannot be directed or regulated. Also, it would be futile to prescribe such technical details as the size of the diaphragmatic aperture or the length of exposure used in fluoroscopy. This and other related aspects of radiation protection will have to remain in the domain of medical education. That such a leadership can be provided is indicated in the decision of the American Academy of Pediatrics (1961) in which it advises all pediatricians to discontinue fluoroscopy of their patients "whenever possible."[26] The importance of education in radiation protection was emphasized by Taylor[27] in 1956 and recently by Chadwick.[8]

Experience shows that without an understanding of the nature and effects of radiation an adequate appreciation and effective practical application of the principles of radiation protection cannot be expected. A step in this direction has been made in a resolution adopted by the California Medical Association in 1964 which states that ". . . there is currently no assurance that some persons operating medical X-ray equipment have had education or examinations in the use of such"; it urges "the deans of California Medical Schools to include in the medical curriculum instructions in the use and hazards of X-rays and other ionizing radiation sources." This resolution also requests "the State Board of Medical Examiners to ask basic questions in this field of all candidates for licensure."[17]

There can be no satisfactory radiation protection in the diagnosgic application of X-rays without more thorough education of all practicing physicians in diagnostic roentgenology.[2,28] One of the main purposes of this paper is to direct attention to the importance of this concept. Emphasis is placed on the responsibility of the nonradiologist-physician and on the use of chest fluoroscopy as a major source of radiation exposure. It is not suggested that fluoroscopy as a method of examination be abandoned, but a limitation of its use is proposed. Neither is the purpose of this paper to discourage nonradiologist-physicians from practicing diagnostic roentgenology. It seems, however, that there is a need for a revision of our thinking and practices. The question the medical profession faces in this matter can probably be phrased as follows: Either will this profession find ways toward a more thorough education in radiology (both in clinical diagnostic roentgenology and radiation biology) in the course of the general training of physicians, or diagnostic roentgenology should be practiced only by such physicians who have formal training and qualifications in this field. Particular importance is attached to chest fluoroscopy in this proposition.

### Conclusions

Fluoroscopy as an independent diagnostic procedure should be abandoned.

Examination of the chest by fluoroscopy, with possible rare exceptions, should be preceded by roentgenography.

Correct indication and the selection of the right procedure, both in fluoroscopy and radiography, are very important factors in radiation protection.

(*Continued on page 394*)

# Basic Concepts of (Re)habilitation of Hard-of-Hearing and Deaf Persons*

ALFRED G. CONSTAM, M.S.E.E.†

In order to plan a good rehabilitation and habilitation program we need to know the effects of a hearing loss. Most hearing losses which can not be helped medically or surgically indicate that there is not enough speech information coming through the ear. This loss of hearing has 2 different aspects which occur simultaneously: loss of sensitivity and loss of discrimination.

Loss of sensitivity means that the sounds are not loud enough. Loss of discrimination means that people are not able to discriminate among different types of sounds. This loss creates confusion. A typical reaction of a patient is: "I can hear but I cannot understand." Group discussions with much noise are difficult for this type of hearing loss.

What can be done about it? Loss of sensitivity can be compensated for by the use of a hearing aid. A hearing aid contains a microphone, an amplifier, and an earphone. The latter supplies the ear with amplified sound.

### Hearing Aids

Hearing aids have some characteristics which are often overlooked. Due to the inertia of the microphone's and earphone's diaphragms, hearing aids are good for the low frequencies (low pitch) and for slow changes as they occur in vowels. A hearing aid gives features very important for the understanding of speech, such as rhythm, stress, duration, number of syllables, and, depending on the hearing, vowel and consonant distinction. Hearing aids are poor in amplifying fast noise-bursts and weak high-frequency consonants (for example "th" in "thin"). That is the reason why it is difficult to understand speech with a hearing aid in the beginning. Practice improves the situation significantly.

Another feature of hearing aids is that when the microphone's and earphone's diaphragms come to a strong vibration through noise the vibration continues for a while after the noise has stopped. It sounds like a reverberation. A knowledge of these points makes it possible to understand the complaints of hearing-aid wearers. Nevertheless, a hearing aid when properly selected, fitted, and used is a very useful and successful device, especially when nothing else can be done.

### Improvement of the Understanding of Speech

I want to stress the fact that the hard-of-hearing person can do very much to improve his understanding of speech. There are some rules which help:

Rule 1. The distance between the microphone of the hearing aid and the talker should be as close as possible. Stand or sit on the correct side of the talker when wearing a behind-ear or eyeglass hearing aid (with microphone not in front).

Rule 2. Arrange the situation so that light falls on the face of the talker in order that one may be able to lipread (every person lipreads to a certain degree).

Rule 3. Reduce noise and reverberation as much as possible by the use of rugs and wood and shut off background noise from radio and TV.

Rule 4. Learn to listen to the low-frequency features of speech, like rhythm, stress, number of syllables, duration, and consonants, voiced or unvoiced.

The following rationale lies behind these statements:

Rule 1. If the talker is close to the microphone the speech is coming through the hearing aid much stronger than the noise, and thus the reverberation effects are small. It is not too well known that hearing aids are sensitive to the origin of the sound (direction-sensitive). Body-type hearing aids pick up sounds best coming from the front and practically no sounds coming from the back. Behind-ear hearing aids are most sensitive to sounds coming from the back on the side that the hearing aid is worn and a little less sensitive to sounds coming from the front side on which the hearing aid is worn (hearing aid worn left, talker left side in front). The situation is extremely bad when a talker is opposite the hearing aid (hearing aid left, talker right in front). It is therefore necessary to have the talker on the same side and in front of where the hearing aid is worn.

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* The opinions expressed herein are the personal ones of the author.

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Rule 2. When the light is on the talker's face it is possible to see the lips and facial movements, but when the light is shining in the hard-of-hearing person's face he will not see enough of the talker's face. Remember to put the light in the position for taking a photographic picture of the talker's face. The hard-of-hearing person must lipread in a noisy situation because the hearing aid alone does not give enough information.

Rule 3. Background noise is far worse for hearing-aid users than for normals, because each sound is amplified with reverberation effects. During the time the noise has a certain intensity the speech is cut out, which means a heavy information loss. Heavy rugs, curtains, wood, and special ceiling plates reduce the reverberation. It helps to cut off all noise sources (radio, TV, sometimes air-conditioner). The ideal condition is still a face-to-face conversation with correct light.

Rule 4.[1] Learning to listen to low-frequency features is very important. We hear many characteristics of speech which help for understanding, for example, duration, rhythm, stress, number of syllables, low-frequency vowel characteristics, and low-frequency consonant characteristics. When hearing is good no attention is paid to these factors, and therefore they have to be learned.

In order to be able to understand the aims of lipreading and auditory training we have to broaden the concept of understanding speech.

## Principles of Error Reduction[2]

When a person starts talking and we have no idea about what and we have to guess what he is going to say, we have a few thousand words to choose from. Each feature we know about a word eliminates a great number of possibilities from which to choose. The more features we know the more possibilities are eliminated, until finally we have only 1 choice left, the correct word. For example, when the word has 3 syllables the number of possible selections is reduced. Knowing the subject which is being talked about (as another feature) reduces further the number of possible choices or errors. When we ask a question with the answer to be "yes" or "no," we have to decide only which of the 2 possibilities has been spoken. We may summarize this by formulating a fundamental principle: The more features we know about something spoken, the better we can understand, because the number of possible errors or confusion is reduced.

Let us look at the features we get through hearing, lipreading, and those which help the brain to make better use of an incomplete message. When a person is talking even most deaf persons with a hearing aid will hear rhythm, stress, number of syllables of a word, duration, and differentiation between vowel and consonant groups, whether voiced or unvoiced. The better the hearing, the better the differentiation between vowel groups and consonant groups.

The features which we lipread are facial movements, expressions, and differentiation between some vowel groups and some consonant groups.

What features help the brain to make sense of an incompletely understood message? These may sometimes be influenced separately: familiarity with the spoken subject, context, intelligence, mental alertness, ability to concentrate, familiarity with the talker, knowledge of language, vocabulary, structure of language, correct selection of words based on knowledge of frequency of occurrence, ability to synthesize, and use of restricted vocabulary (airline pilots communicate over radio with a very restricted vocabulary) such as questions which require an answer of only "yes" or "no."

How can we learn to make the best use of the factors mentioned above? We can train our hearing (auditory training) and lipreading and try to use these factors as much as possible.

Why is hearing training helpful? When the hearing changes, the sounds appear different to the brain. They do not correspond to the sounds stored in the memory. An identification of sounds is therefore difficult. With a hearing aid the sounds are different, and also a hearing aid brings back sounds which have not been heard for a long time. Therefore, the sounds have to be rememorized. If keen listening is developed, sounds can be heard and discriminated which otherwise would not be differentiated. A very good practical book is Browd's "The New Way to Better Hearing."[3] The hearing training covers the range from gross sound differentiation to very fine ones such as similar vowels and consonants.

Why is lipreading so helpful? It gives an additional way of differentiation between vowels and consonants. There are deaf people who use lipreading as their chief means of communication and who are quite successful at it. Due to the fact that not all consonants and vowels can be distinguished, the features which help to make sense of an incompletely understood message are very important. Unfamiliar names are rarely understood, even by people with normal hearing.*

### Optimal Use of the Factors Completing an Incompletely Understood Message

This is a highly individual matter to be thought through for each individual. Three examples may illustrate this point:

A woman suffered a slowly progressing hearing loss due to age. It came to a point where she was not able to understand what was said at her own party for friends. So next she invited each person alone, asked about hobbies and so on, and knew then what the topics would be and what each person would talk about. At the next party when she invited them all again she was able to follow the conversations successfully because she was familiar with the lines the conversation would take.

A sales person did not understand the questions of the customers and got easily upset. After improvement of the layout, whereby most questions became unnecessary, and in lighting conditions, making it possible to see the customer's face, the troubles were solved.

A deaf person came to a new job. The most frequent and important words had been written down and explained. With routine and increasing familiarity the difficulties decreased rapidly.

To summarize, use ingenuity. To treat this phase thoroughly would be far beyond the scope of this article, but most people can improve their situation greatly by watching these factors.

### Special Problems of Deafness

There are 2 major groups: people who become deaf after acquiring speech and people who became deaf before they learned to speak. People who become deaf after having learned to speak are to be considered extremely hard-of-hearing. If they do not hear speech any more their own speech may deteriorate. As soon as the first signs show up, immediate speech corrections have to take place before wrong patterns of habitude are formed too deeply.

Problems of deafness before acquiring speech are the most difficult because these persons have no language background on which most of the complementary information is based. Without early language the mental development is delayed. It must be emphasized that early training[4] starting from the age of about 12 to 15 months gives the best possible results. After a certain age it is much harder to teach speech. All people who have learned a foreign language know that it is difficult to get rid of an accent unless the foreign language is taught very early. The sounds of the different languages are quite similar, and so we can imagine how much more difficult it is to produce speech sounds at all when they were never learned.

What should be done if a heavy hearing loss is noticed and medically or surgically nothing can be done? In many cases a child does well with a hearing aid and by watching the lips. Sounds mean something to him. The child, not hearing accurately enough, does not learn to speak correctly without being specifically taught to do so. The sense of touch is used in addition to hearing and watching the lips. The child touches the throats of his mother and his own and tries to match the vibration and corrects according to the mother's or teacher's reaction.

If the child's vocabulary does not increase and progress is too slow due to the limited hearing, the supplemental use of finger-spelling is recommended. Finger-spelling is a manual alphabet.

Good vocabulary is essential for good "lipreading-hearing aid" communication. It is necessary to get professional advice, which can be obtained through hearing clinics. The best thing to do is to enroll the child as early as possible in a preschool in which optimal facilities for training are available. For information about schools and courses write to the Editor of the *American Annals of the Deaf,* Gallaudet College, Washington, D. C. 20002, or Volta Bureau, 1537 35th Street, N.W., Washington, D. C. 20007. For correspondence courses write to John Tracy Clinic, 806 West Adams Blvd., Los Angeles, Calif. 90007.

### Some Further Developments in the Research Stage

A normal child learns to speak by constant imitation of what he hears. The purpose of a visual speech-trainer is to allow a visual imitation. The deaf person tries to match the pattern on an oscilloscope screen which was made by a normal person. The visual speech-trainer† measures electronically some characteristic speech features.

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* For information concerning hearing training and lipreading courses write to Volta Bureau, 1537 35th Street, N.W., Washington, D. C. 20007.

† Designed and built by the writer; J. M. Pickett, Project Director.

R. Orin Cornett, Vice President of Gallaudet College, developed a very interesting system called "Cued Speech."[5] Knowing that not all vowels and consonants can be differentiated properly by lipreading alone, the system provides additional information by hand, making it possible to distinguish properly all vowels and consonants from each other. This system identifies each speech sound correctly, thus eliminating the guessing which is inherent in lipreading alone. It has a considerable training effect in lipreading and gives the deaf a perfect knowledge of how each individual word has to be spoken. I consider this to be a major breakthrough.

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### Changing Concepts in Chest Fluoroscopy—Gondos

(*Continued from page 390*)

In fluoroscopy more emphasis is to be placed on the efficiency in observation and interpretation as a means of protection from excessive radiation.

More teaching of diagnostic roentgenology during the course of the general medical education is proposed as an instrument of radiation protection. The same consideration should be given to some fundamentals in radiation biology.

The manufacturing and purchasing of X-ray equipments which are suitable for fluoroscopy only should be discouraged.

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# Allergy to Insect Stings

## Clinical and Laboratory Studies

SOLOMON E. BARR, M.D.*

ALLERGY TO INSECT STINGS is a very important problem, resulting in many deaths and much disability. In the United States more people die every year from insect stings than from snake bites.[1] Treatment of this problem has proven to be extremely effective. Those of us practicing allergy often see large numbers of patients with insect-sting allergy. This paper summarizes an experience with patients allergic to insect stings and combines some serologic studies in animals rendered allergic to the stinging insects.

### Clinical Study

*Patient selection.* The records of all patients seen from August 1960 through July 1965 on whom treatment was begun for allergy to insect stings were summarized (table 1). These data include only those patients deemed allergic to insect stings and do not include patients with whom injections were never started. A patient was judged clinically allergic to the stinging insect if he had either a generalized reaction or a very large local reaction to the sting. Fifty-eight persons had had constitutional reactions consisting of 1 or more of the following: asthma, shock, loss of consciousness, angio-edema, rhinorrhea, hypotension, nausea, or vomiting. Twenty-four persons had had large local reactions consisting of huge swellings spreading from the site of the sting to involve at least 2 joints if on an extremity. Twenty-four persons had been so sick as to require epinephrine injections. Six of the patients were related to each other. Forty-five patients had a history of other allergies—hay fever, hives, asthma, or eczema.

Identification of the type of insect causing the reaction proved to be extremely difficult. In only 42 of the 91 stings was the offending insect identified with moderate certainty (table 1). Identification was partially aided by the fact that only the honeybee leaves her venom sac at the site of the sting. This may explain the higher number of identifications of the sting being due to the honeybee; 19 of the 42 positive identifications were of honeybee.

**TABLE 1: Summary of Clinical Data on Patients**

| | | |
|---|---|---|
| Age (median): 11 ½ years | | |
| Sex: | | |
| Male | | 54 |
| Female | | 28 |
| Race: | | |
| Caucasian | | 81 |
| Negro | | 1 |
| Type of reaction: | | |
| Constitutional at least once | | 58 |
| Large local only | | 24 |
| Epinephrine required: | | 24 |
| History of other types of allergy: | | 45 |
| First skin test to the suspected insect negative, and second test positive 2 weeks later: | | 4 |
| Constitutional reactions on skin-testing: | | 1 |
| Patients in this series closely related: | | 6 |
| No. stings from type of insect identified with moderate certainty: | | 42 |
| Bee | 19 | |
| Wasp | 6 | |
| Hornet | 3 | |
| Yellow jacket | 14 | |
| Type of insect identified questionably: | | 28 |
| Bee | 12 | |
| Wasp | 9 | |
| Hornet | 5 | |
| Yellow jacket | 2 | |
| Type of insect completely unknown: | | 21 |
| | | 91* |

* The number of stings is greater than the number of patients because several patients had more than 1 sting.

*Skin-testing* (table 2). This was begun with a dilution of either 1/100,000 or 1/10,000 of mixed stinging insect venom depending upon the clinical sensitivity. Intradermal skin-testing was performed with 0.025 ml. and read in 10 minutes on the basis of the size of the wheal—4 pluses to a cm. If negative or equivocal reactions were observed the test was repeated with a 10-fold increase in concentration of the extract. The maximum concentration used was 1/100 because anything stronger was considered a primary irritant. Only reactions of 2+ or better in the 1/1,000 dilution or 4+ in the 1/100 dilution were considered significant. Once the level of skin-testing sensitivity was noted the patient was also tested for each of the 4 types of stinging insects—honeybee, wasp, hornet, or yellow jacket. In only 13 of these patients did one skin test show markedly more positive than the others. The other 69 showed several equally positive skin-test reactions to 2 or more of the insect types. In only 9 patients did 1 significantly positive skin test correlate closely with the clinical description of the stinging insect. Only 1 of the patients on whom skin-testing was performed had a constitutional reaction to the test. Surprisingly, he was a boy who had had only a large local reaction with a sting. Four people had negative skin tests when seen shortly after the insect sting but changed to positive when retested 2 weeks later.

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**TABLE 2: Summary of Skin-test Reactions**

| | No. Patients |
|---|---|
| One test significantly more positive than the others: | 13 |
| Significant tests to several types of insects: | 69 |
| Skin-test reaction and clinical description of insect correlated closely: | 9 |
| Skin-test reaction and clinical description correlated poorly: | 73 |
| First test to the suspected insect negative and reaction positive on retesting 2 weeks later: | 4 |

*Emergency treatment.* In the event of an insect sting, patients were instructed to apply a venous tourniquet above the sting if on an extremity and to go to the nearest physician's office or hospital emergency room. During the first 3 years of this study adults were given a 15 mg. isoproterenol tablet and children a 10 mg. isoproterenol tablet to place underneath the tongue if stung. It has recently become increasingly clear that isoproterenol is a beta-adrenergic agent with no beneficial effect upon shock. Therefore, patients have now been given either an emergency kit of preloaded syringes containing epinephrine* or a 5 c.c. aerosol inhaler containing epinephrine.†

*Treatment with allergy extracts* (table 3). Hyposensitizing injections were begun with 0.10 c.c. of the most dilute solution which gave a positive response. All but 3 of the patients received a mixture of all 4 types of stinging insect (table 3-A). These 3 were patients who were much more sensitive to 1 insect both by a clear-cut history and skin-testing. The dosage of all patients was increased by weekly injections either to the maximum they could tolerate or to 0.5 c.c. of the 1/10 dilution. Maintenance injections were then begun every 4 weeks and were later increased to every 5 or 6 weeks as tolerated. There were very few reactions to the injections, the most common being a slight swelling at the site of the injection lasting for a few hours. One person had several constitutional reactions and discontinued injections.

**TABLE 3: Summary of Treatment**

| | No. Patients |
|---|---|
| A. Type of extract: | |
| Patients treated with extracts of all 4 types of insects | 79 |
| Patients treated with extract of 1 type of insect | 3 |
| B. Subsequent history: | |
| Patients lost to follow-up | 9 |
| Patients not stung since treatment started | 38 |
| Patients stung since treatment started | 35 |
| | **No. Stings** |
| C. Results of treatment: | |
| Stings after treatment started with no difficulty | 83 |
| Stings with constitutional reactions milder than before | 2 |
| Stings with constitutional reaction of equal severity as before treatment | 1 |
| Stings with increased severity of reaction | 0 |
| Total number of stings: | 86 |

*Results of treatment.* Follow-up data have been obtained on 73 patients (table 3-B). Thirty-five patients have been restung since beginning treatment. Some people were stung on more than 1 occasion, and 86 stings were recorded (table 3-C). Eighty-three stings were experienced without difficulty except for a minimum amount of redness at the site of the sting. Two people experienced constitutional reactions, but these were judged to be much milder than previous ones. One person experienced a generalized reaction of about the same severity as before starting injections.

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* Purex Emergency Kit, supplied by Purex Laboratories, Staten Island, N. Y.

† Medihaler-Epi 5 c.c., a product of Riker Laboratories, Northridge, Calif.

### Serologic Studies with Animal Sera*

*Material and methods.* The extracts employed were specially prepared highly concentrated solutions of either honeybee 110,000 PNU,† wasp 100,000 PNU, hornet 160,000 PNU, and yellow jacket 60,000 PNU. Animal serum was obtained by injecting 1 c.c. of each of these 4 types of insect extracts with 2 c.c. of complete Freund adjuvant into the buttock of a rabbit—a total of 6 c.c. Eight days later an aqueous mixture of 0.5 c.c. of each of the 4 types of insect extracts was injected without adjuvant intravenously into an ear vein. One month after the initial injection blood was withdrawn by intracardiac puncture. Ouchterloney plates were prepared according to the method of Holbert.[2] Then 0.10 ml. of the insect antigen was placed in the peripheral wells, and 0.20 ml. of the immune rabbit sera was placed in the central well. Passive cutaneous anaphylaxis (PCA) tests were performed according to the method of Fisher.[3] The serum was injected into the abdominal skin of 500 Gm. guinea pigs. Five hours later each animal was injected intracardially with a mixture of 1 ml. of the extract and 2 c.c. of Evan's blue (table 4).

**TABLE 4: Results of Passive Cutaneous Anaphylaxis (Rabbit-immune Serum in Guinea-pig Skin)**

| Challenged with | Serum Site | Saline Control | Interpretation |
|---|---|---|---|
| Honeybee 55,000 PNU | Positive | Positive | "Histamine shock" |
| Honeybee 27,500 PNU | Positive | Negative | Positive reaction |
| Hornet 80,000 PNU | Positive | Slightly positive | Probable positive reaction |
| Hornet 40,000 PNU | Positive | Negative | Definite positive reaction |
| Wasp 50,000 PNU (2 occasions) | Positive (2×) | Negative (2×) | Positive |
| Yellow jacket 30,000 PNU | Negative (2×) | Negative (2×) | Negative |

*Results of studies with animal sera.* Precipitin bands were observed between the rabbit serum and the bee, wasp, and hornet antigens. The line with yellow jacket antigen was too faint to be readily defined. In figure 1 a separate line can be seen for bee, wasp and hornet, with a common precipitin line for the hornet and the bee. Positive passive cutaneous anaphylaxis tests (table 4) were shown for honeybee, hornet and wasp, but not for yellow jacket antigen. The first time that the honeybee extract was injected the animals exhibited a generalized "histamine shock" with blue nose and eyes and severe dyspnea. Much blueness occurred at all test sites, which made interpretation impossible. Repeating the tests with ½ the amount of antigen produced a positive test. A milder histamine shock was noted with the hornet extract.

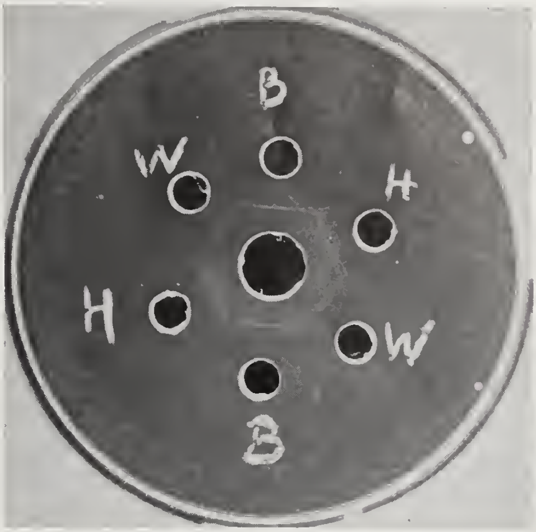

FIG. 1. Ouchterloney plate preparation with immune rabbit serum. Center—rabbit serum. B—honeybee extract; W—wasp extract; H—hornet extract. Note common precipitation line between honeybee and wasp and the individual lines for all 3 insects.

### Discussion

*Patient selection.* There is little question that people who have had severe generalized reactions from a few insect stings should receive allergy desensitization. There is, however, question as to the advisability of giving insect desensitization to people who have experienced only large local reaction to insect stings. The average individual exhibits some swelling at the site of an insect sting. Histamine, serotonin, and kinins which can cause nonspecific swelling have been found in Hymenoptera venom.[4] Loveless[5] has noted nonspecific reactions to insect extracts. The Insect Study Committee of the American Academy of Allergy[6] has noted a growing tendency among the members to consider a huge local reaction as an indication of allergy and to treat as such. It is interesting that the only patient in this series who developed a constitutional reaction from skin-testing had had "only" a large local reaction. I consider swelling extending beyond 2 nonadjacent limb joints to indicate allergy. All patients in this series had a combination of either a generalized reaction from an insect sting or a huge local reaction combined with a positive skin test to 1 or more of the stinging insects.

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* This work was performed at the Roosevelt Hospital Institute of Allergy, New York, N. Y.

† One PNU (protein nitrogen unit) equals 0.00001 mg. of phosphotungstic acid precipitable nitrogen per ml.

*Types of antibodies.* By immunizing rabbits Foubert and Stier[7] were readily able to demonstrate rabbit antibodies to the stinging insects. The first case of a human exhibiting precipitating antibodies was that of McCormick[8] who in 1963 found these antibodies in the postmortem serum of an individual who had died shortly after being stung by a paper wasp. By modifying the method of Ouchterloney precipitin analysis, Brown[9] has now been able to demonstrate precipitin lines to various hymenoptera in a number of human sera. Figure 2 demonstrates the precipitin lines found in the postmortem serum of a child who died shortly following an insect sting.*

*Types of extracts.* It is the opinion of Loveless[5] that because the patient has been stung with the venom sac instead of the entire insect the patient should be immunized only with the venom sac. However, the work of many authors[10-14] indicates that there are some antigens common to the body, others to the sting sac, and still others only to the venom of the insect. At present all the commercially available insect allergens are made from the entire body. Many workers[5, 7, 10-14] have found some antigens specific to 1 type of insect and other antigens common to several types. As already mentioned, in only 42 of the 91 pre-immunization stings suffered by the patients in the present series were the patients "reasonably" sure what had stung them (table 1). This correlated well with 1 skin test much more positive than the others in only 9 cases. It is my opinion that a person should be immunized to a mixture of stinging insects unless he can make a positive identification of the offending insect and only that 1 insect type is reactive on skin-testing.

*Discontinuing treatment.* It is difficult to know when to stop allergy injections to the stinging insects. Several cases have been mentioned[15, 16] of patients who received insect stings without difficulty while on allergy injections but then died when restung after the injections had been discontinued. The Academy of Allergy Insect Committee reported 106 persons who had been restung after varied intervals of lapsed hyposensitization.[17] Protection has been reported as continuing from 18 years to less than 1 year. At present there is no good reliable test for clinical immunity. Brown[18] gradually increased the time between injections to as much as 16 weeks with apparently good results.

*Refractory period.* Occasionally, during the period immediately after an acute allergic insult a person will not react on skin-testing to the suspected insect. This condition occurred with 4 patients who were skin-tested shortly after their sting with negative results and when retested 2 weeks later had positive skin tests (table 2). Shaffer[19] reported that this refractory period may last 10 to 14 days following the sting. Therefore, it is advisable to wait 2 weeks after the sting has occurred to perform the skin tests.

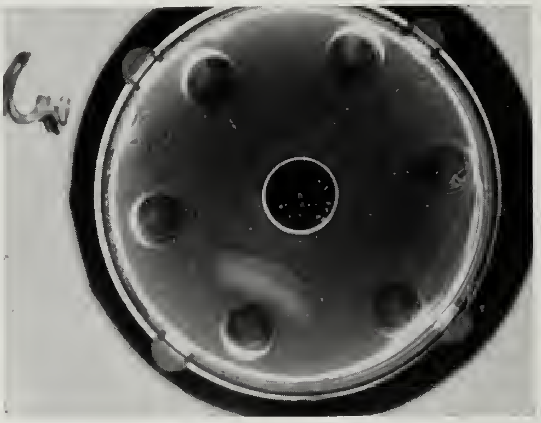

**FIG. 2. Ouchterloney plate preparation with serum obtained postmortem from a child who died of anaphylactic shock following a honeybee sting. Center—the child's serum. Extract in the well at 7 o'clock is honeybee. The other wells contain extracts from other hymenoptera. (Courtesy of Lt. Colonel J. E. Stauch.)**

*Results of treatment.* The Insect Study Committee of the American Academy of Allergy has kept a record of 2,606 insect-sting sensitizations.[6] At the time of the March, 1965 report 647 persons had been restung after varying degrees of hyposensitization. Of these, 580 reported improvement, 41 were unchanged, and 26 were worse. There were 763 untreated and later restung patients. Of these, 72 reported improvement, 199 were unchanged, and 492 experienced reactions of increased severity. To summarize, 89.6 per cent of the treated but only 9.4 per cent of the untreated patients improved with subsequent stings. In the present series (table 3) no patient had a reaction more severe than had occurred prior to treatment, and only 1 person had a reaction of equal severity.

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* This previously unpublished photograph was obtained through the courtesy of Lt. Colonel J. E. Stauch, M.C., U. S. Air Force, Andrews Air Force Base, Maryland.

### Conclusion and Summary

Allergy to insect stings is a serious problem causing more deaths and disability in this country every year than do snake bites. Records of 82 patients who had received insect sting immunization have been analyzed. Patient identification of the exact type of stinging insect was poor. Sixty-nine of 82 people gave positive skin tests to more than 1 type of insect. Over a 5-year period 86 stings were reported subsequent to beginning allergy injections. In 83 there was virtually no reaction, in 2 there was a reaction of lesser severity, and in only 1 was there a reaction of equal severity. A rabbit was hypersensitized to the 4 types of stinging insects. Its serum gave both positive Ouchterloney precipitin lines and positive passive cutaneous anaphylaxis reactions to honeybee, wasp and hornet, with some precipitin lines common to more than 1 insect.

Serologic studies of many authors have demonstrated antigens common to both body and venom sac and antigens common to more than 1 type of insect. All reports indicate that immunization to the stinging insects affords a high degree of protection against reaction to subsequent stings. The conclusion is that: (1) A patient who has suffered an allergic reaction from an insect sting should be immunized to the stinging insects; (2) this should be to the insect mixture unless rigid criteria of insect identification and skin-testing are met; and (3) this may have to be continued for an indefinite period of time but with an increasing interval between injections.

I wish to acknowledge the advice and assistance of Drs. William Sherman, Arsenio Vivera and Jarek Fisher with the serologic studies; of Dr. J. E. Stauch for permission to use figure 2; and of Drs. Sherman and Halla Brown for advice in the preparation of the manuscript.

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## Patients Needed at Clinical Center

The coöperation of physicians is requested in the referral of patients for a study of ataxia telangiectasia syndrome being conducted by the Medical Neurology Branch, National Institute of Neurological Diseases and Blindness, at the Clinical Center of the National Institutes of Health in Bethesda, Md.

Ataxia telangiectasia syndrome is an affliction of infants and young children characterized by ataxia, oculocutaneous telangiectases, and susceptibility to infections. Selected patients with this syndrome will be admitted to the Clinical Center for study of their neurological and immune status, particularly immunoglobulin metabolism, and for evaluation of endocrine function. Upon completion of their studies patients will be returned to the care of the referring physician who will receive a full report of the studies done.

Physicians interested in having their patients considered for admission to this study may write or telephone Dr. Dale E. McFarlin, Clinical Center, Room 10-N-310, National Institutes of Health, Bethesda, Md. 20014; telephone: 656-4000, Ext. 65930.

# Treatment of Diabetes Insipidus in Children with Synthetic Lysine-8-Vasopressin Nasal Spray

WELLINGTON HUNG, M.D., F.A.A.P.*

THE LONG-TERM TREATMENT of diabetes insipidus has been either the intramuscular injection of Pitressin® Tannate in (peanut) Oil or the nasal insufflation of crude posterior pituitary powder. Both of these preparations are of animal origin. The treatment of choice in children has been the intramuscular injection of Pitressin Tannate in Oil.[1] This medication has the disadvantages of having to be administered parenterally every 1 to 3 days, and occasional reactions to peanut oil occur. A serious complication of this therapy is water intoxication which results from excessive administration of this long-acting preparation. Crude posterior pituitary powder has a disagreeable aroma, frequently causes nasal irritation, and may be ineffective.

The synthesis of vasopressin[2, 3] led to a commercial method of producing a nasal spray containing synthetic lysine-8-vasopressin.[4] The present report deals with our experience in the use of lysine-8-vasopressin (L-8-VP) nasal spray in 5 children with diabetes insipidus.

## Materials and Methods

Five children with diabetes inispidus have been treated to date. The diagnosis was documented in all patients by appropriate studies.[1] All of the patients were males and ranged in age from 2 to 16 years. Eosinophilic granuloma was present in 3 patients; the etiology was unknown in 2. Three patients were started on L-8-VP nasal spray as soon as the diagnosis of diabetes insipidus was established, 1 patient had been treated with pitressin tannate in oil, and 1 patient had received posterior pituitary powder in nasal insufflation. L-8-VP nasal spray was provided in 5 ml. (50 I.U./ml.) squeeze-bottle containers.† The nasal spray was administered either by the patient himself or by a parent. The patients were instructed to increase both the frequency and number of squirts as needed to prevent polydipsia and polyuria. They received the L-8-VP nasal spray every 2 to 6 hours during the day and at bedtime.

TABLE 1: Data of Patients with Diabetes Insipidus Treated with Lysine-8-Vasopressin Nasal Spray

| Patient | Age | | Duration of Diabetes Insipidus Before L-8-VP | L-8-VP Nasal Spray Treatment | | | Daily Urine Volume (L) | |
|---|---|---|---|---|---|---|---|---|
| | Yrs. | Mos. | | No. Times Administered | Squirts per Nostril | Duration of Therapy (months) | Time of Diagnosis | With L-8-VP |
| J. H. | 8 | 5 | 3 years | 7 | 3 | 20 | 2.6–4.7 | 1.1–1.3 |
| R. K. | 14 | 10 | 10 years | 5 | 4 | 19 | 2.9–3.9 | 1.4–1.6 |
| D. T. | 16 | 10 | 1 month | 10 | 4 | 19 | 2.0–4.6 | 1.3–1.7 |
| G. B. | 15 | | 1 month | 5 | 3 | 7 | 5.3–6.8 | 1.5–1.8 |
| J. D. | 2 | | 3 months | 8 | 6 | 5 | 2.3–2.9 | 0.8–1.0 |

## Results

The 5 patients have been treated for periods of time ranging up to 20 months (table 1). The L-8-VP nasal spray was effective in decreasing urine volume and increasing concentrations in all of the patients. Only 1 patient had occasional nocturia once a night. Water intoxication was not seen in any of the patients. The antidiuretic action of L-8-VP nasal spray was noted in all patients within 1 hour. No hypertensive response to the spray has been detected. There have been no significant adverse reactions to date. A minor adverse effect was minimal nasal irritation in 1 patient. L-8-VP nasal spray was temporarily ineffective in patients with nasal congestion due either to an upper respiratory infection or allergic rhinitis. During these periods the maintenance dosage was increased approximately 3-fold or parenteral therapy with Pitressin Tannate in Oil was reinstituted temporarily.

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† Supplied through the kindness of Dr. Paul S. Arcese, Sandoz Pharmaceuticals, Hanover, N. J.

### Discussion

Our results indicate that L-8-VP nasal spray is an effective and apparently nonirritating agent in the long-term treatment of diabetes insipidus in children. The dosage necessary to control polydipsia and polyuria is variable. The spray has been shown to be rapidly absorbed and is cleared from the plasma in 3 to 5 hours.[5] This may account for the fact that patients with more severe degrees of diabetes insipidus need a larger dosage and greater frequency of administration. During periods of nasal congestion the spray becomes less effective. Our observations confirm previous reports in adults of the efficacy and lack of adverse effects of L-8-VP nasal spray.[5, 6, 7] The spray allows the patient to be treated without the discomfort and inconvenience of parenteral Pitressin Tannate in Oil or the aroma and nasal irritation of posterior pituitary powder. The benefits of L-8-VP nasal spray are its simplicity and ease of administration, particularly for the parents of the young child with diabetes insipidus, the lack of significant adverse effects, and the satisfactory control.

### Summary

Five children with diabetes insipidus have been treated effectively with lysine-8-vasopressin nasal spray. The spray was administered every 2 to 6 hours during the day and at bedtime. The dose administered was that necessary to control polyuria. Only 1 patient had occasional nocturia once a night. The only minor adverse effect was minimal nasal irritation in 1 patient. A transient decrease in effectiveness was noted during periods of nasal congestion due to upper respiratory infection or allergic rhinitis. The use of the spray is recommended in the treatment of diabetes insipidus because of its ease of administration, its effectiveness in the control of polydipsia and polyuria, and the lack of significant adverse effects.

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## Enrollment in Federal Employees' Health Benefits Program

The Civil Service Commission reports that the number of persons covered under the Federal Employees Health Benefits program increased by 700,000 in 1965–1966, to a total of 7.5 million—about 4 per cent of the total population of the United States.

In a report just released on enrollment in the program as of November 30, 1966, CSC said more than 2.4 million employees and annuitants and 5.1 million of their dependents are now participating in the program.

Currently, benefits provided by the program are running at about $41 million a month. About 1.6 million covered persons receive benefits during a year. Total monthly cost of the program is now $52.5 million, with employees paying 66 per cent and the Government the remaining 34 per cent.

Results of the November 1966 "open season" indicate:

— Practically all eligible employees are now enrolled in the program.

— The majority of employees and annuitants were already enrolled in a plan and option with which they were satisfied.

— The majority of enrollees still desire the greater benefits offered by the more expensive high options of the plans, although there is a slight indication that enrollment in the low options is receiving more consideration than before. Some of this increased interest stems from annuitants eligible for Medicare dropping to low options to supplement Medicare coverage. About 7,900 of the 286,000 enrolled annuitants changed to low options during the "open season."

# A Prospective Study of Digitalis Toxicity in a Large City Hospital*

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Digitalis toxicity continues to be a clinical problem of major importance not only because of its frequent occurrence based on the universal use of the drug but also because of the concurrent administration of potent diuretic agents and shifts in body electrolytes. In city hospitals, such as ours, the problem is further compounded by the advanced age of a large proportion of the patients, their inability to adhere to a strict dosage schedule, and their propensity to take "extra pills" whenever their sense of well-being declines.

It is the purpose of this presentation to describe the results of a prospective study of 60 cases observed over a 24-month period on the wards and the Cardiac Clinic of the District of Columbia General Hospital and to emphasize the high incidence of digitalis toxicity and its unusual, often misinterpreted manifestations.

## Material and Methods

All patients of this study were seen by at least one of us. Based on our experience with the population of our hospital and the difficulties in obtaining adequate and specific information related to the previous medications, it was decided to keep under observation and off digitalis not only those patients who exhibited classical symptoms and signs but also those with suggestive evidences of digitoxicity. All mentally confused or semicomatose patients who were under treatment with "heart pills" and for a "heart condition" or exhibited electrocardiographic evidence of arrhythmia were observed as suspects for various lengths of time. Eventual inclusion in the study was based on adequate history of excessive digitalis alone or in combination with diuretic therapy obtained from the patient, his relatives or the medical personnel of his referring institution, and unequivocal data gathered during the observation period.

Documentation of diagnosis of digitoxicity was sought through the following procedures: (1) recovery from signs and symptoms within a reasonable length of time after cessation of therapy under close observation, or more gradually during follow-up visits in the case of the outpatients; (2) inadvertent resumption of digitalis therapy by physicians not directly involved in the study and the resultant recurrence of signs and symptoms of digitalis intoxication, or exacerbation of the existing ones; and (3) deliberate redigitalization after withdrawal of the drug for 2 or more weeks and when the patient was free of all symptoms suspected of digitoxicity with consequent recurrence or emergence of typical features of toxicity.

By necessity, a high degree of reliance was placed upon our own observation of the patients while off therapy and/or after resumption of digitalis treatment at a dosage equal or less than the dose originally considered responsible for toxicity. The study may therefore be considered somewhat subjective.

Altogether, 130 patients in highly suggestive circumstances were selected for observation. Seventy of them were subsequently excluded from the study because confirmation of digitalis toxicity could not be achieved with certainty or the suggestive symptoms and signs proved to be more plausibly attributable to such factors as uremia or liver disease. For instance, patients exhibiting isolated, complete heart block while taking digitalis were kept under close surveillance off digitalis for several weeks. Five of them were rejected because of persistence of A-V block and 2 were eventually admitted to the study when their heart block was shown to be related to the use of digitalis.

Of the 60 patients included in this study 36 were female and 24 were male, with ages ranging from 30 to 90 years. About two-thirds of the patients

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**TABLE 1: Presenting Symptoms Plotted Against Digitalis Preparation and Dosage, Serum Potassium, Prior Diuretic Therapy, Underlying Heart Disease, and Treatment of Toxicity**

| | Digitalis Preparation | | | Dosage | | | Concomitant K Rx | | Concomitant Diuretic | | Underlying Heart Disease | | | | | Rx of Toxicity | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Presenting Symptoms | Leaf | Digoxin | Digitoxin | Average | Average | Average | Yes | No | Yes | No | PMD | HCVD | ASCVD | PHCVD | RHD | Stop digitalis | Potassium | Quinidine | Pronestyl |
| | 18 | 37 | 5 | 5 | 35 | 20 | 33 | 27 | 36 | 24 | 9 | 19 | 21 | 4 | 7 | 60 | 17 | 6 | 6 |
| A. Arrhythmia 51* | 16 | 32 | 3 | 3 | 36 | 12 | 26 | 25 | 31 | 20 | 9 | 18 | 18 | 4 | 2 | 51 | 16 | 2 | 6 |
| PAC (2) | 1 | 1 | | | 2 | | 2 | | 2 | | | | 1 | 1 | | 2 | | | |
| PAT (8) | 2 | 6 | | | 4 | 4 | 6 | 2 | 2 | 6 | 3 | 1 | 2 | 2 | | 8 | 3 | | |
| Atrial fibrillation (6) | 2 | 3 | 1 | | 3 | 3 | 2 | 4 | 3 | 3 | | 2 | 2 | 1 | 1 | 6 | 3 | | 1 |
| PVC (15) | 4 | 10 | 1 | 1 | 9 | 5 | 9 | 6 | 10 | 5 | 7 | 4 | 2 | | 2 | 15 | 7 | 3 | 1 |
| Ventricular tachycardia (3) | 1 | 1 | 1 | | 1 | 2 | 1 | 2 | 1 | 2 | | 1 | 2 | | | 3 | 1 | | 3 |
| Ventricular fibrillation (1) | | 1 | | | 1 | | 1 | | 1 | | 1 | | | | | 1 | | | 1 |
| Complete A-V block (16) | 3 | 12 | 1 | 2 | 11 | 3 | 10 | 6 | 9 | 7 | 1 | 7 | 8 | | | 16 | 2 | | 1 |
| Incomplete A-V block (6) | 2 | 3 | 1 | | 1 | 5 | 4 | 2 | 2 | 4 | 2 | 1 | 2 | 1 | | 6 | 1 | | |
| A-V dissociation (8) | 3 | 5 | | | 5 | 3 | 7 | 1 | 6 | 2 | | 3 | 3 | 1 | 1 | 8 | 4 | 1 | 3 |
| B. Progressive CHF 11* 5 | 3 | 8 | | 1 | 4 | 6 | 6 | 5 | 7 | 4 | 2 | 4 | 4 | 1 | | 11 | 8 | | 1 |
| C. G.I. 29* | 9 | 19 | 1 | 2 | 15 | 12 | 16 | 13 | 21 | 8 | 4 | 10 | 9 | 2 | 4 | 29 | | 2 | 1 |
| Anorexia (18) | 8 | 9 | 1 | 2 | 8 | 8 | 8 | 10 | 15 | 3 | 3 | 6 | 3 | 2 | 4 | 18 | | | |
| Nausea (17) | 5 | 12 | | 2 | 8 | 7 | 11 | 6 | 12 | 5 | 2 | 5 | 6 | 3 | 1 | 17 | | 1 | |
| Vomiting (16) | 5 | 10 | 1 | 1 | 7 | 8 | 9 | 7 | 11 | 5 | 2 | 5 | 6 | | 3 | 16 | | 1 | |
| D. CNS 15* | 5 | 7 | 3 | 1 | 10 | 4 | 7 | 8 | 7 | 8 | 2 | 4 | 4 | 3 | 2 | 15 | 5 | 1 | 2 |
| Dizziness (3) | 2 | 1 | | | 2 | 1 | 1 | 2 | 2 | 1 | | 1 | | 1 | 1 | 3 | 1 | | |
| Insomnia (3) | 1 | 2 | | | 3 | | 1 | 2 | 1 | 2 | | | | | 3 | 3 | 1 | | |
| Confusion (7) | | 5 | 2 | 1 | 3 | 3 | 4 | 3 | 3 | 4 | | 1 | 4 | 1 | 1 | 7 | 2 | 1 | 1 |
| Lethargy to semicoma (5) | 3 | 1 | 1 | | 3 | 2 | 2 | 3 | 2 | 3 | | 3 | | 2 | | 5 | 1 | | 2 |
| Syncope (3) | 2 | 1 | | | 2 | 1 | 2 | 1 | 2 | 1 | | 1 | | | | 3 | 2 | 2 | |
| E. Weakness 5* | 1 | 4 | | 1 | 4 | | 2 | 3 | 4 | 1 | 1 | 2 | | | 2 | 5 | | | |
| F. Hiccough 3* | | 3 | | 1 | 2 | | 1 | 2 | 2 | 1 | | 1 | | | | 3 | 2 | 2 | |
| G. Gynecomastia 1* | | 1 | | | | 1 | 1 | | 1 | | | | 1 | | | 1 | | | |

N.B. Figures marked by asterisks show total number of patients presenting the symptoms recorded adjacent to them. Numbers appearing in the top horizontal column subjacent to the headings represent number of patients related to those headings. Figures in parentheses on the vertical column adjacent to presenting symptoms depict number of patients with those symptoms.

Abbreviations:

PAC = Premature atrial contraction
PAT = Paroxysmal atrial tachycardia
PVC = Premature ventricular contraction
CHF = Congestive heart failure
G.I. = Gastrointestinal symptoms
CNS = Central nervous system symptoms

(40, or 66 per cent) were between the ages of 60 and 80 years.

Arteriosclerotic and hypertensive diseases of the heart (ASH, HCVD) were the most frequent underlying heart diseases encountered among this group, 21 and 19 respectively. Primary myocardial disease (PMD) as defined in our previous report[1] accounted for 9 cases and rheumatic heart disease for 7. These last 2 categories were encountered primarily among the younger subjects (30–50 years). In the remaining 4 cases pulmonary hypertensive cardiovascular disease (chronic cor pulmonale) was the primary cardiac diagnosis. Considered of aggravating or precipitating influences were renal disease with uremia in 12 cases, alcoholic cirrhosis in 5, and diabetes mellitus in 4.

## Results (Table 1)

*Digitalis preparation.** The most common preparations used in this hospital are digoxin (Lanoxin®) and digitalis leaf U.S.P. Thirty-seven patients were taking digoxin, 18 were maintained on digitalis leaf, and only 5 were taking digitoxin. In the digoxin-treated group the daily dose leading to toxicity was found to be less than the average in

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* Accepted average daily maintenance dosages: leaf U.S.P., 0.1 Gm.; digoxin, 0.25 mg.; digitoxin, 0.1 mg.; average digitalizing dose of lanatoside C, 1.6 mg.

5, average in 21, and greater than the average in 11. Of the 18 patients taking digitalis leaf 1 patient was receiving 0.1 Gm. every second day, 12 patients were taking the average dose, and the remaining 5 received 0.2 Gm. daily. Of the 5 digitoxin-treated cases 3 were receiving 0.2 mg. and 2 0.1 mg. daily. The major manifestations of arrhythmia, gastrointestinal and central nervous system symptoms were equally distributed among patients receiving leaf and digoxin.

*Duration of toxicity.* The duration of toxicity as judged by the persistence of symptoms and signs after initiation of the observation period varied from 1 to 16 days. It was directly related to the severity of the heart disease and to the complicating factors such as uremia. One 56-year-old woman with HCVD and uremia was receiving 0.125 mg. of digoxin every second day. Toxicity persisted for 12 days and was manifested by gastrointestinal symptoms and arrhythmia. Symptoms recurred twice on resumption of similar dosage. As the renal insufficiency improved she was able to tolerate the same dosage without toxic manifestation.

*Contributory factors.* Thirty-six patients were receiving parenteral mercurials or oral thiazide derivatives concurrently with digitalis (for serum electrolytes see table 2). Thirty-three patients were receiving supplemental oral daily doses of KCl. Serum potassium (K) was normal in 50 patients, and only 8 patients had values between 1.9 to 3.5 mEq./L. Two patients had serum K of 6 to 8 mEq./L on repeated determinations, and both suffered from underlying renal disease. All patients with electrolyte disturbances were receiving diuretic therapy.

**TABLE 2: Serum Electrolytes and Blood Urea Nitrogen**

Serum Electrolytes (mEq./L) and Blood Urea Nitrogen (mg./100 ml.)

| Less than Normal | | Normal* | More than Normal |
|---|---|---|---|
| $K^+$ | 8 | 50 | 2 |
| $Na^+$ | 12 | 42 | 6 |
| $Cl^-$ | 13 | 42 | 5 |
| BUN | — | 35 | 25 |

* $K^+$ 3.5 to 5.5; $Na^+$ 135 to 145; $Cl^-$ 99 to 106; BUN 6 to 20.

Among the 25 patients with elevated blood urea nitrogen (BUN) ranging from 40 to 100 mg./100 ml., only 11 had underlying renal disease. In the remaining 14 patients no underlying renal disease was found on the basis of routine laboratory and roentgen investigations, and the serum BUN returned to normal following cessation of digitalis and diuretic therapy. Transient elevation of BUN was distributed equally in both digoxin- and leaf-treated groups and was attributed to dehydration and poor renal perfusion.

### Presenting Symptoms and Signs (Table 1)

*Cardiac manifestations.* Cardiac arrhythmias were noted in 51 patients (85 per cent) and included all of the known major types except atrial flutter. In 19 patients arrhythmia was the only manifestation of digitoxicity. Four deaths during the first 72 hours of hospitalization were directly attributed to digitalis, producing final episodes of ventricular fibrillation in 1 patient and ventricular tachycardia in the other 3. Of great interest was the strikingly high incidence of complete A-V block, having been present in 16 cases. Four such patients were admitted initially to the psychiatric wards because of mental confusion and were found on subsequent observations to be suffering from digitoxicity.

Persistent congestive heart failure (CHF) caused by digitoxicity was noted in 11 cases (18 per cent).

*Gastrointestinal (G.I.) symptoms.* Twenty-nine patients (48 per cent) had gastrointestinal symptoms with anorexia, nausea and vomiting, occurring in that order of frequency. The gastrointestinal disturbances were unrelated to the type of digitalis preparation used or the local effect of KCl. Fifteen patients were taking KCl tablets, and 14 were taking digitalis alone or in combination with a diuretic agent. G.I. symptoms were the sole manifestation of excess digitalis therapy in 5 patients.

*Central nervous system (CNS) symptoms.* Neuropsychiatric manifestations were noted in 15 patients. In 3 they were the only features of digitoxicity and included insomnia alone in 2 and dizziness unrelated to posture and heart rate in 1. In the remaining 12 patients CNS manifestations were associated with cardiac, G.I., or both cardiac and G.I. symptoms. Of the 7 patients with varying degrees of mental confusion, amnesia, or hallucinations, 5 had digoxin-induced complete heart block. Three of them exhibited Stokes-Adams seizures. A varying degree of lethargy to semicoma was encountered in 5 patients. Eleven patients with the more serious CNS manifestations were between the ages of 60 and 80 years.

*Unusual manifestations.* Apathy and extreme weakness not attributable to arrhythmia occurred in 5 patients. They were directly related to digitalis therapy and disappeared upon withdrawal of the drug. Only 1 patient was receiving diuretics. Serum electrolytes were normal in all of these patients. Three patients manifested persistent hiccough which was proved to be related to digitalis. All were receiving digoxin. Unilateral gynecomastia developing over a 4-month period was noted in 1 patient with heart block inadvertently receiving 0.5 mg. of digoxin daily for at least 1 year. The complete A-V block was documented for a period of 6 months prior to inclusion in the study. Following discontinuation of digoxin, normal A-V conduction was restored within 16 days, but gynecomastia persisted until the conclusion of this study.

## Discussion

Almost 2 centuries after the introduction of digitalis by Withering proper digitalization of a severely ill patient remains an art, particularly with the concomitant use of the new and powerful diuretics in an aging population. Nevertheless, as stated by Kay,[2] "No substitute for the digitalis is on the horizon. They are of incalculable value in the everyday life of millions of human beings. Perhaps with more care and wisdom in the use of these drugs, many patients may be helped a little more and a few a great deal more."

The unique feature of digitalis is its narrow therapeutic-toxic ratio approaching unity. In terminal stages of cardiac decompensation, toxicity may even precede optimal therapeutic action, and it may therefore be impossible to use digitalis profitably or at all.[3] On the other hand, in the absence of heart disease large doses may be taken without serious ill effects as exemplified by Bickel's report[4] of a 36-year-old woman without heart disease who survived a suicide attempt by taking 50 mg. of digitoxin.

Data concerning morbidity of digitalis administration have generally been gathered from the hospitalized patients. The incidence of mild to severe toxicity among this group varies from 7 to 20 per cent.[5, 6] In the present study the incidence of digitoxicity was not determined because only a fraction of the total hospital population taking digitalis could be studied.

Mortality directly attributed to digitalis varies from 4 to 11 per cent,[5, 7, 8] and was 7 per cent (4 patients) in this study. In another 4 patients deaths occurred during the period of toxicity, but digitalis could not be incriminated wholly because of the coexistence of other diseases. Two of these patients died suddenly as they were recovering from digitoxicity.

Almost any type of atrial and ventricular arrhythmia can occur in digitalis intoxication,[7, 9, 10] and the incidence of arrhythmia in general has been found to be as high as 95 per cent.[8] In our group 51 patients (85 per cent) manifested single or combined rhythm disturbances. It is highly probable that continuous monitoring of these patients would have yielded an even higher incidence.

Much emphasis has been placed on the high frequency of digitalis-induced paroxysmal atrial tachycardia (PAT) with variable A-V block.[11, 12] Only 13 per cent of our patients exhibited this arrhythmia. On the other hand, our finding of complete heart block as the most common arrhythmia (16 cases, or 27 per cent) is indeed interesting. The ventricular pacemaker was in the A-V junction in all these cases. The addition of the 8 cases of A-V dissociation with junctional pacemaker to this group yields the astonishingly high incidence of 24 cases (40 per cent) for the nodal rhythm, a finding which is in accord with some previous reports.[13, 14, 15] Figure 1 depicts 2 of the cases of nodal rhythm.

Atrial fibrillation caused by digitalis was found in 6 patients (10 per cent), 3 of them with rapid ventricular rates exceeding 100/min. and 3 with slow rates under 60/min. DeGraff[16] stated that "the development of atrial fibrillation in a patient formerly in normal sinus rhythm is an important toxic manifestation of digitalis." In our series all 6 patients reverted to normal sinus rhythm between 2 to 4 days after withdrawal of digitalis (figure 2). A large number of patients (18, or 30 per cent) were in atrial fibrillation because of their heart disease. Digitoxicity in this group was manifested by extreme slowing with irregularity of the ventricular beats in 8 patients, ventricular regularity due to a slow nodal rhythm in 10, and ventricular bigeminy in 5 (figure 3).

Among the 13 patients with premature ventricular beats (PVC) bigeminal rhythm associated with atrial fibrillation was noted in 5. None had rheumatic heart disease as has been postulated.[17] Three patients with multifocal PVC's died in ventricular tachycardia and 1 of ventricular fibrillation.

In severely damaged hearts congestive heart failure may be due to the toxic effects of excessive digitalis, a therapeutic paradox.[3, 17] Eleven such cases were encountered in our group. Withdrawal of digitalis resulted in improvement in all.

Nausea and/or vomiting have been mentioned among the most frequently occurring symptoms of digitoxicity.[7, 8] Anorexia may or may not precede the onset of emesis.[18] Twenty-nine patients (48 per

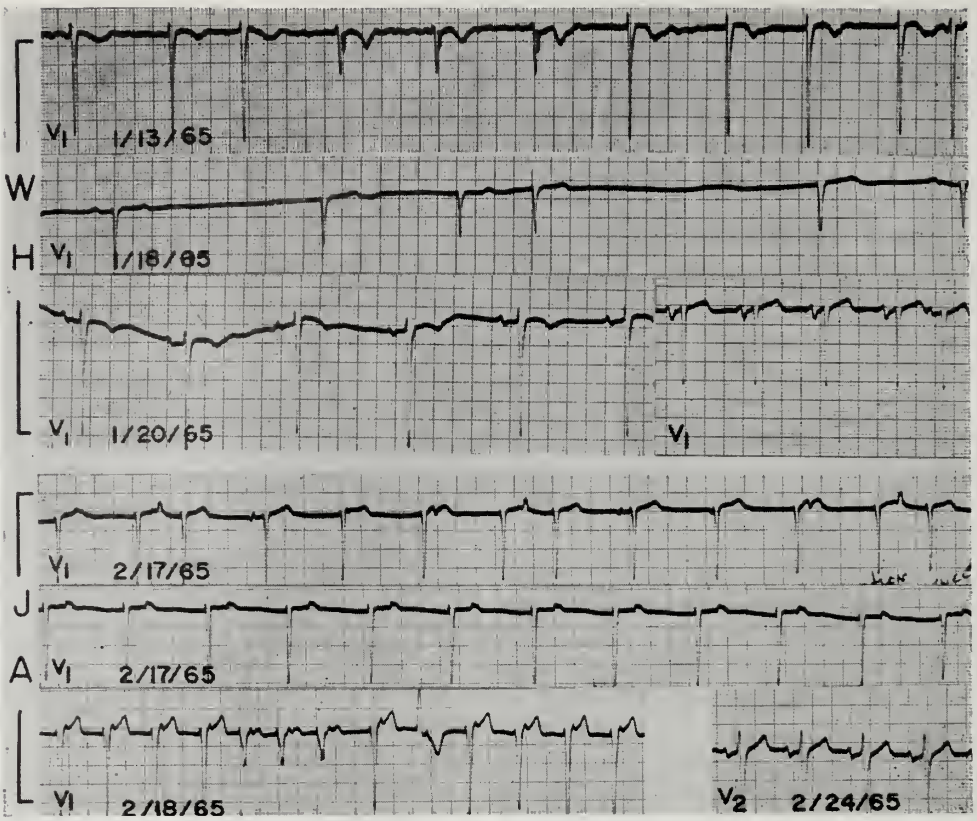

FIG. 1. W. H., 64-year-old man with aortic regurgitation. Top row, atrial fibrillation with run of regular A-V nodal rhythm in beats 4 to 6 occurring after 2.5 mg. digoxin given over a period of 4 days; drug discontinued at this time. Middle row, taken 5 days after withdrawal of digitalis. Rhythm now that of slow sinus rhythm with periods of sinus arrest terminated by nodal escapes. Bottom row, taken 2 days later, shows sinus bradycardia on left. Short strip to right of this row was taken several days later when all evidence of toxicity had abated.

J. A., 77-year-old woman with aortic and mitral regurgitation. Top row, A-V dissociation while receiving 0.1 Gm. of digitalis leaf daily plus hydrochlorothiazide—atrial rate 64/min., ventricular rate 75/min. Note interference beats 3, 8 and 13. Middle row, same day, persistent A-V nodal rhythm at rate of 86/min. Bottom row, left strip, nodal tachycardia 1 day later; right strip, return to normal sinus rhythm 6 days later.

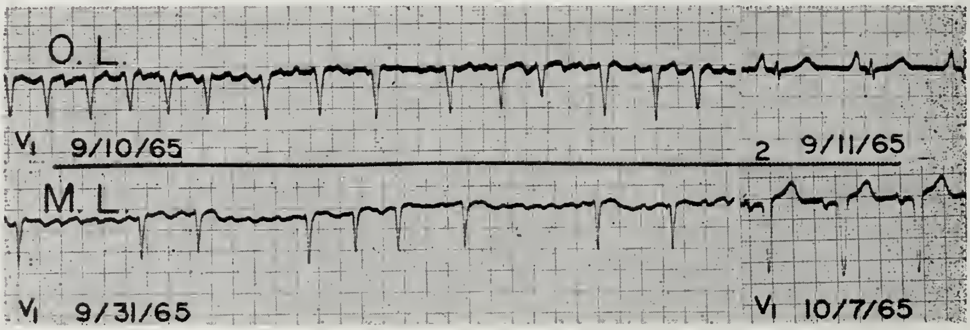

FIG. 2. Top row, O. L., 52-year-old man with primary myocardial disease; atrial fibrillation with rapid ventricular rate of about 130/min. after 1.2 mg. lanatoside C given intravenously over 12-hr. period. Normal sinus rhythm next day shown on right of strip. Bottom row, M. L., 63-year-old woman with hypertensive cardiovascular disease, found to have atrial fibrillation with relatively rapid ventricular rate averaging 80/min., receiving digitalis leaf 0.1 Gm. daily plus KCl 1 Gm. daily. After cessation of digitalis and increase of KCl to 3 Gm. daily rhythm became normal as shown on right of strip.

cent) experienced gastrointestinal manifestations of digitoxicity. In 4 the progression of symptoms was prevented by early cessation of the drug following the appearance of anorexia. However, in 11 patients nausea and vomiting not preceded by anorexia marked the onset of digitoxicity.

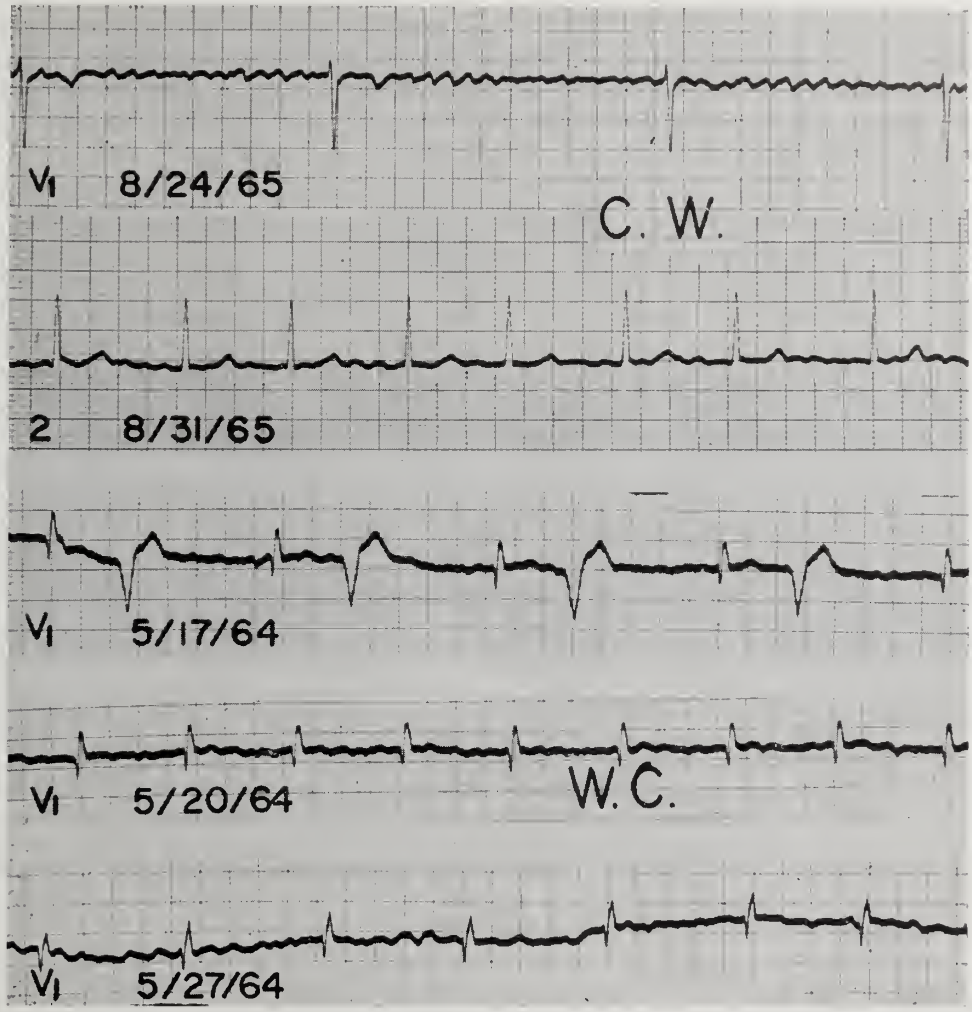

**FIG. 3.** C. W., 31-year-old woman with severe rheumatic mitral regurgitation. Top row, atrial fibrillation with very slow ventricular rate of about 28/min. while receiving digitalis leaf 0.1 Gm. daily plus hydrochlorothiazide 50 mg. daily; complaint of fatigue and recurrence of symptoms of failure. Tracing on second row 7 days after cessation of digitalis and use of potassium showing more rapid ventricular rate, at this time completely asymptomatic.

W. C., 63-year-old woman with arteriosclerotic heart disease. Top row, atrial fibrillation with ventricular bigeminy. Basic beats 1, 3, 5, 7 and 9 suggesting autonomous A-V nodal pacemaker, taken while receiving 0.2 mg. digitoxin daily; middle row recorded 3 days after digitalis was discontinued. Except for disappearance of PVC's, basic mechanism of atrial fibrillation and autonomous A-V nodal forms occur at rate of 80/min. Bottom row recorded 7 days later shows complete disappearance of signs of autonomy of ventricles, being now controlled by the atria in usual fashion and beating irregularly.

Neuropsychiatric manifestations of digitalis, particularly in elderly patients, have been pointed out by Batterman and Gutner,[19] and digitalis delirium has been described in detail by Church et al.[20] From mild dizziness to profound coma, neuralgia, transient mental aberrations, hallucinations, and delusional psychoses have been recognized more readily since that time.[2, 4, 5, 8, 15, 18-21] Fifteen patients (25 per cent) in our series presented a variety of neuropsychiatric manifestations. Insomnia in 3 patients was reproducible on several occasions. Four patients were admitted to the psychiatric wards because of psychotic reactions and hallucinations. Despite constant search for the visual symptoms of digitalis toxicity we were unable to obtain a clear history in any of our patients.

Intractable hiccough in 3 patients was of special interest. To our knowledge only 1 report of such instance has appeared in the literature.[4] Despite the elevated BUN in 2 cases hiccough disappeared in 3 to 5 days following withdrawal of digitalis and recurred upon redigitalization. The third patient had hypertensive cardiovascular disease without renal insufficiency.

Gynecomastia, unilateral or bilateral, in both sexes during digitalis therapy has been observed.[7] LeVimm[22] demonstrated the direct effect of digitalis in producing gynecomastia. Although enlargement of the left breast was of recent onset in our case and cardiotoxic manifestation of digitalis disappeared following withdrawal of the drug, the gynecomastia remained unchanged for the ensuing 4 months of observation.

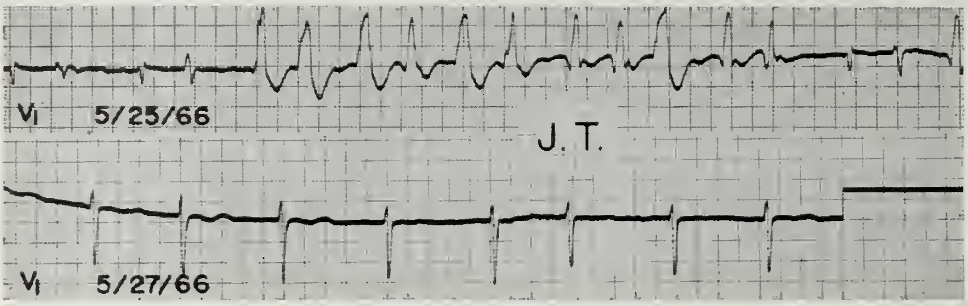

**FIG. 4. J. T., 76-year-old man with arteriosclerotic heart disease admitted to Neuropsychiatric Ward because of recurrent convulsive seizures followed by postictal unconsciousness. Top tracing, atrial fibrillation with short run of ventricular tachycardia obtained by the consulting medical resident (Dr. A. Sidhu, George Washington University Division, D. C. General Hospital), who suspected digitalis toxicity. After recovering consciousness, patient admitted to having taken digitoxin 0.4 mg. daily plus hydrochlorothiazide 50 mg. daily for 2 weeks for treatment of congestive heart failure; immediately treated with intravenous procainamide plus KCl with improvement. Tracing 2 days later, depicting atrial fibrillation with ventricular rate of about 70/min. shown on bottom row.**

It is generally accepted that there are no significant differences in the spectrum of toxic manifestations among the various glycoside preparations.[5, 7, 20] In our group 18 patients (30 per cent) were receiving digitalis leaf and 37 patients (62 per cent) digoxin, and our study indicates that there is no difference in the toxic manifestations, specific organ predilection, or the duration of toxicity related to the preparation used. This is in accord with the work of others.[23, 24] Only 20 patients (33 per cent) were taking more than the average daily doses of the digitalis preparation. The so-called average daily dose (in 58 per cent) producing toxicity emphasizes the point that individual requirements of digitalis are unpredictable, and, in effect, that the process of digitalization constitutes a biologic titration, during which the dose that will achieve the maximum therapeutic action without causing toxicity must be determined.[25]

Widespread use of new and powerful diuretics, especially in elderly people, is a well-known precipitating factor. Rapid diuresis has been incriminated in as many as 20 to 37 per cent of the cases of digitalis intoxication.[7, 25, 26] Thirty-six patients (60 per cent) in our series were treated with diuretics. In 24 patients (40 per cent) receiving average or even smaller daily doses of digitalis diuretic therapy was thought to be the primary precipitating or contributory factor.

Random serum potassium determinations in patients on combined diuretic and digitalis therapy may create a false impression in relation to digitalis intoxication.[11, 15] It has been demonstrated that in experimental animals a 5 to 10 per cent decrease of body potassium reduces the amount of digitalis required to produce ventricular tachycardia by about 60 per cent.[27] On the other hand, the influence of serum pH and the Na/K ratio on the pharmacologic effect of potassium has been emphasized by Bellet.[28] In our group only 8 patients (13 per cent) had serum potassium values less than 3.5 mEq./L on repeated determinations.

## Treatment

Selection of the various therapeutic approaches was left to the discretion of the house physicians directly involved in the management of the patients. Generally speaking, treatment became more vigorous with the more severe arrhythmias. Thus, 37 patients with mild rhythm disturbances were observed off digitalis, and all recovered without any specific therapy. Seventeen patients exhibiting more severe arrhythmias received potassium therapy orally (14 cases) or intravenously (3 cases), and all recovered. Of these, only 8 patients had low serum potassium values. The remaining 6 patients with life-threatening arrhythmias received the combination of potassium and procainamide intravenously (figure 4). Of these, 3 patients with ventricular tachycardia and 1 with ventricular fibrillation died, while the remaining 2 with runs of multifocal PVC's survived.

## Summary and Conclusions

Sixty patients with digitalis intoxications were studied prospectively in a 24-month period, and the pertinent data have been presented.

Toxicity occurred not only with average and larger doses but also with smaller-than-average doses, especially in the presence of renal and pulmonary diseases and of advanced heart disease.

Neuropsychiatric manifestations were common, especially in the older individuals, and were usually not ascribed to digitoxicity. Awareness of these manifestations and a high index of suspicion for digitoxicity in the psychotic or obtunded geriatric patient are necessary for correct diagnosis.

Intractable congestive heart failure in a digitalized patient with underlying heart disease may be a manifestation of digitalis toxicity.

No significant difference was found in the clinical presentation and duration of toxicity related to the preparation used.

Normal serum potassium levels did not contradict digitalis toxicity.

Results of this study indicate that a policy consisting of viewing as suspects all digitalized patients who have bizarre as well as inexplicable symptoms may be justified. Accordingly, it is suggested that emergence of arrhythmias of any type, persistent heart failure, gastrointestinal symptoms, weakness, insomnia, irritability, psychosis, mental obtundation, etc. be regarded as signs of digitoxicity and that the patients be observed closely while off the drug.

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# PRESIDENT'S PAGE

## OFFICE ETIQUETTE

Recurring complaints from patients, addressed to the Grievance Committee of the Medical Society, focus attention on certain details of office procedure which demand comment. The importance of maintaining good public relations, dignity, courtesy, and thoughtfulness in professional conduct cannot be overemphasized. Unfortunately, it is evident that some practitioners overlook certain elementary but vitally significant features of doctor-patient relationship which create misunderstanding, discontent, and resentment. These situations result in time-consuming, stressful review by the Grievance Committee and sometimes in initiation of lawsuits that reflect discredit on the entire professional community. Let us consider 3 areas which constitute sources of frequent patient complaints.

Chaperonage during examination of female patients is essential. The presence of a nurse or female assistant cannot be eliminated when performing gynecological examinations. Such procedures are uncomfortable and embarrassing to many patients; they should *never* be done in the absence of a suitable assistant. Accusations of improper or unprofessional behavior are automatically obviated when this precaution is observed. It is distressing how often neglect of this fundamental rule is the origin of legitimate patient complaint.

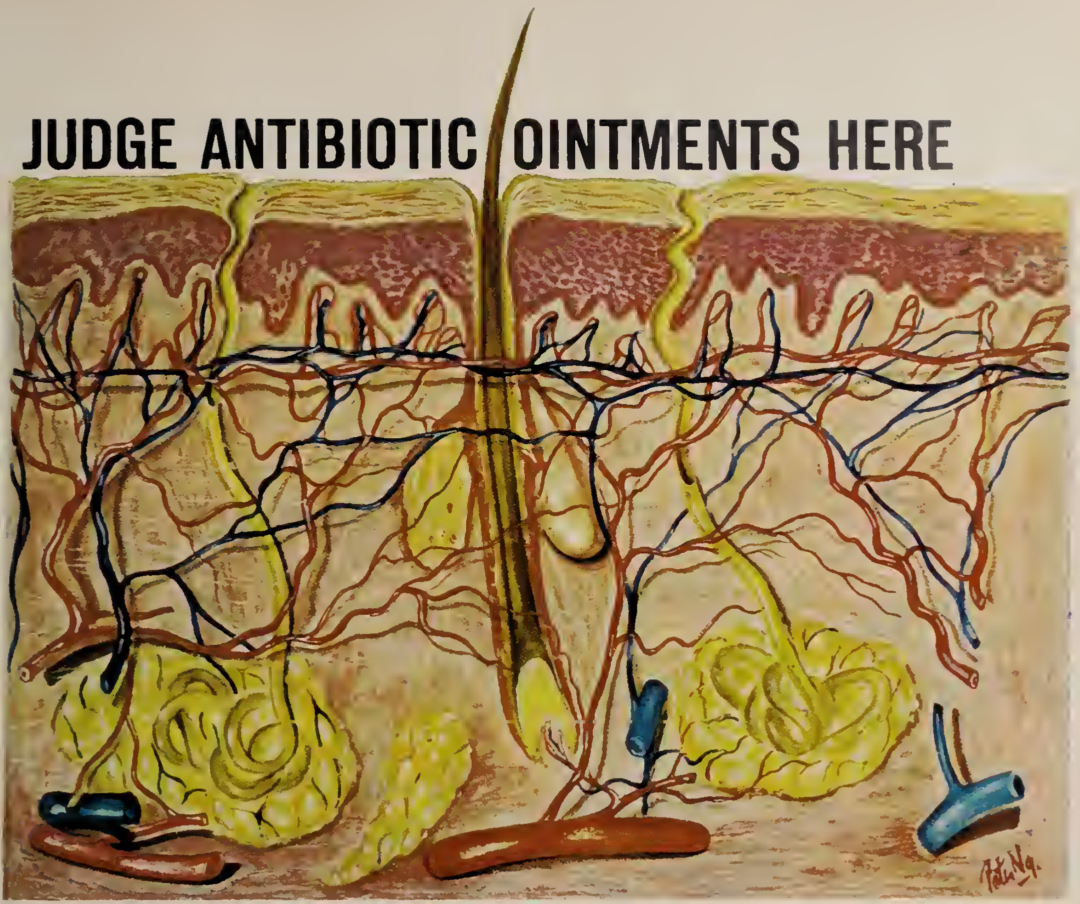
Indignation expressed by a patient upon receipt of a bill is a most repetitive complaint addressed to the Medical Society's Grievance Committee. This is a problem simply avoided. Discussion and explanation of charges before the service is rendered would tend to eliminate this source of dissatisfaction. We do not buy "a pig in a poke" in any other area of our economy—why should the medical profession employ a cloak of secrecy? We surely are not ashamed of the value we place on our services. We are not out to mulct the public. We flatter ourselves that our charges are reasonable under the circumstances surrounding the service and the patient's economic position. With this in mind it is mandatory that the patient be informed of what is expected as payment together with a detailed explanation of what he is paying for. Time and again such complaints have been resolved by explanation—but only after dissolution of confidence in the doctor and after engendering resentment and destruction of faith in the medical profession. A few minutes of courteous attention to a sick or anxious person's concern about finances will pay great dividends in creating good will rather than anger and castigation.

Another important aspect of fulfilling our responsibility is to guarantee constant availability of medical attention. No physician should leave his practice without providing alternate coverage. Adequate answering service and the coöperation of an associate or a colleague in the same specialty are easy to obtain and must never be neglected. These facets of medical care if omitted may not become cause for suit and may not come to the attention of the Grievance Committee, but they are among the most frequently voiced complaints of our patients.

Review your procedures with these points in mind to improve your performance and to help convince the public that we are honestly trying to serve to the satisfaction and betterment of all the community.

Henry D. Ecker

# JUDGE ANTIBIOTIC OINTMENTS HERE



**Results on skin are final proof of any topical antibiotic's effectiveness**

**No in vitro test can duplicate a clinical situation on living skin.** 'Neosporin' (polymyxin B—bacitracin—neomycin) Ointment has consistently proven its effectiveness in thousands of cases of bacterial skin infection. The spectra of the three antibiotics overlap in such a way as to provide bactericidal action against most pathogenic bacteria likely to be found topically. Diffusion of the antibiotics from the special petrolatum base is rapid since they are insoluble in the petrolatum, but readily soluble in tissue fluids. The Ointment is bland and nonirritating.

**Caution:** As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

**Contraindications:** This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

**Supplied:** Tubes of 1 oz., ½ oz. with applicator tip, and ⅛ oz. with ophthalmic tip.

Complete literature available on request from Professional Services Dept. PML.

**'NEOSPORIN'®**
brand

**POLYMYXIN B-BACITRACIN-NEOMYCIN**
**OINTMENT**

**BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N.Y.**

# Why these 7 patients with
# moderate to severe anxiety
# may respond better to Mellaril

### 1. The agitated patient.

Anxiety—particularly that beyond th
range of minor tranquilizers—fr
quently is expressed as gross moto
restlessness, fidgetiness and purpos
less movements, and may erupt in
aggressive behavior. Mellaril is a
most a specific for those patien
whose anxiety follows such a patter

### The psychosomatic patient.

e family physician is rarely given
e diagnostic luxury of a classic,
tbook "anxiety state." Most often
must probe for anxiety masked by
unctional disorder—or which exac-
bates a somatic problem. Double-
nd evaluations have demonstrated
at Mellaril can be a significant ad-
nct in the treatment of such patients.

### The patient under tuational stress.

llaril helps the patient deal with
esses of everyday life. Nonhabitu-
ng, it can be given for extended pe-
ds of time. It does not "separate"
e patient from practical problems
d pressures, does not induce eupho-
or a fuzziness which can compro-
nise the ability to cope with reali-
ties. Rather, it helps the patient move more competently in his daily world by eliminating useless tension, by allowing him to conserve emotional resources and energies, and to direct them against the problems really worth worrying about.

### 4. The menopausal patient.

The woman who sees change of life as the end of useful life requires support from both family and family physician. Whether the psychological impact of menopause is directly related to hormonal changes, or merely coincidental, is debatable, but estrogenic therapy is frequently inadequate. Mellaril is a useful aid for these patients and, alone, or in combination with reduced estrogen dosage, will help ease the menopausal misery.

### 5. The previously hospitalized psychiatric patient.

Such a patient may still require the type of medication he has been accustomed to, but because he is no longer in a controlled setting the acceptable level of adverse reactions must be lower. In such circumstances Mellaril is perhaps the drug of choice.

### 6. The agitated geriatric.

Tranquilizer therapy in the elderly patient always involves special (or at least accentuated) problems: the possibility of drug-induced ataxia, hypotension or depression, for example, assumes an additional significance. These reactions have rarely been observed in geriatric patients treated with Mellaril.

### 7. The constantly returning patient.

The anxiety patient who has not responded to a minor tranquilizer is not very likely to benefit from your minor tranquilizer of second choice. A major tranquilizer, such as Mellaril, may be indicated in such patients.

**Contraindications:** Severely depressed or comatose states from any cause, and in association with or following MAO inhibitors; severe hypertensive or hypotensive heart disease.
**Precautions:** Hypersensitivity reactions (e.g., leukopenia, agranulocytosis) and convulsive seizures are infrequent. Pigmentary retinopathy has been observed where doses in excess of those recommended were used for long periods of time. May potentiate central nervous system depressants, atropine, and phosphorus insecticides. Where complete mental alertness is required, administer the drug cautiously and increase dosage gradually. In addition, orthostatic hypotension (especially in female patients) has been observed. Epinephrine should be avoided in treatment of drug-induced hypotension.
**Side Effects:** Pseudoparkinsonism and other extrapyramidal disorders are infrequent; drowsiness, especially in high doses early in treatment, may occur; nocturnal confusion, dryness of the mouth, nasal stuffiness, headache, peripheral edema, lactation, galactorrhea, and inhibition of ejaculation are noted on occasion; photosensitivity and other allergic skin reactions may occur but are extremely rare.
*Before prescribing, see package insert for full product information.*

## in moderate to severe anxiety, 25 mg. t.i.d.

# Mellaril®

## (thioridazine)

SANDOZ

Bartholin's gland
Periurethral glands
Cervical glands
Flagyl®.....
brand of
metronidazole
Seminal vesicles
Bladder
Prostate gland

# Destroys Trichomonads Wherever They Are

**Flagyl** seeks out the sites where trichomonads hide. Only a systemic agent can. Flagyl does, selectively and effectively.

Flagyl destroys trichomonads in the inner crypts, glands and cavities of the genitourinary tract in both women and men. Consequently, Flagyl is capable not only of curing trichomoniasis in women but also of preventing reinfection.

Correctly used, with due attention to repeat courses of treatment for resistant, deep-seated invasion and to the presumption of reinfection from male consorts, Flagyl has repeatedly produced up to 100 per cent cure in large series of patients.

When the diagnosis of trichomoniasis is positive, Flagyl is positive.

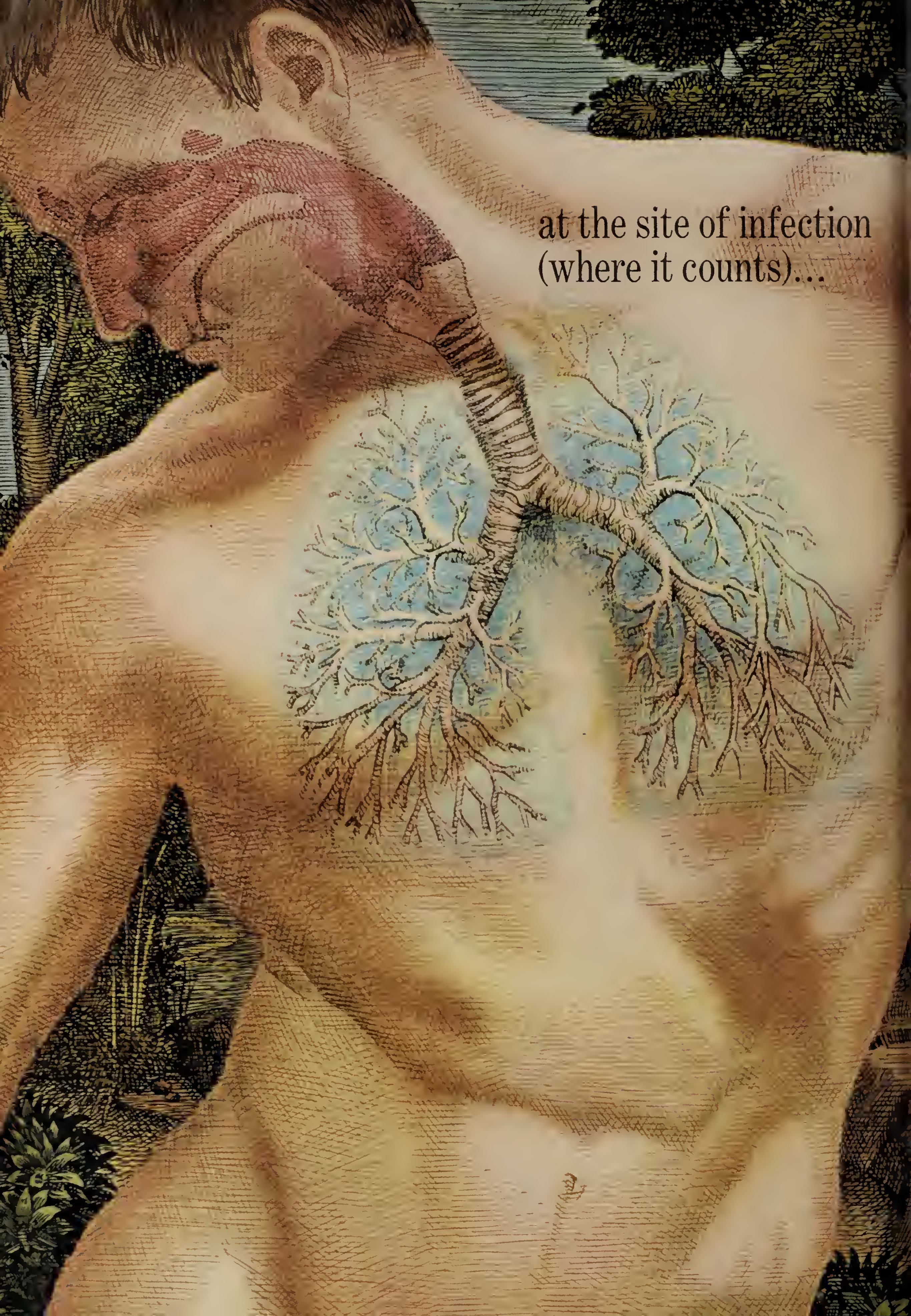
*Dosage and Administration* – In *women:* one 250-mg. oral tablet three times daily for ten days. A vaginal insert of 500 mg. is available for local therapy when desired. When used, one vaginal insert should be placed high in the vaginal vault each day for ten days; concurrently two oral tablets should be taken daily.
In *men* in whom trichomonads have been demonstrated: one 250-mg. oral tablet twice daily for ten days.

*Contraindications* – Pregnancy; disease of the central nervous system; evidence or history of blood dyscrasia.

*Precaution*–Complete blood cell counts should be made before, during and after therapy, especially if a second course is necessary.

*Side Effects*–Infrequent and minor side effects include nausea, metallic taste, furry tongue and headache. Other effects, all reported in an incidence of less than 1 per cent, are diarrhea, dizziness, vaginal dryness and burning, dry mouth, rash, urticaria, gastritis, drowsiness, insomnia, pruritus, sore tongue, darkened urine, anorexia, vomiting, epigastric distress, dysuria, depression, vertigo, incoordination, ataxia, abdominal cramping, constipation, stomatitis, numbness of an extremity, joint pains, confusion, irritability, weakness, flushing, cystitis, pelvic pressure, dyspareunia, fever, polyuria, incontinence, decreased libido, nasal congestion, proctitis and pyuria. Elimination of trichomonads may aggravate candidiasis.

SEARLE *Research in the Service of Medicine*



at the site of infection
(where it counts)...

# Ilosone® provides more antibacterial activity than any other oral erythromycin

**Acid stable, better absorbed . . . Ilosone produces faster, higher, more prolonged blood levels, even in the presence of food[1-3]**

Because it is the most active form of oral erythromycin, Ilosone can help assure consistently greater antibacterial activity at the site of infection. Ilosone produces peak antibacterial blood levels two to four times those of other erythromycin preparations.[1,2] Not only are these levels attained earlier, but they are maintained for much longer periods. Even the presence of food does not seem to affect the activity of Ilosone.[1,3]

In the treatment of patients with bacterial infections susceptible to erythromycin, Ilosone has compiled an excellent therapeutic record. Since it exerts its greatest activity against gram-positive organisms, it is particularly useful in common respiratory and soft-tissue bacterial infections. Ilosone kills—not merely inhibits—streptococci, pneumococci, and more strains of staphylococci than any other macrolide antibiotic. This bactericidal action, coupled with the high antibacterial levels attained, makes Ilosone especially valuable in patients with low host resistance, such as infants, debilitated individuals, and diabetics.

Ilosone has shown no cross-resistance with penicillin and may be effective against organisms that have become resistant to that agent. Despite its high antibacterial activity, Ilosone has demonstrated a low incidence of side reactions. Blood dyscrasias, ototoxicity, and tooth staining have not been observed. Infrequent cases of drug idiosyncrasy, manifested by a cholestatic jaundice, have occurred, but there have been no known definite residual effects.

**Now available:**
New! Ready-mixed Ilosone Liquid 125! (Contains erythromycin estolate equivalent to 125 mg. erythromycin base per 5-cc. teaspoonful.)

700970

**Ilosone®**
**Erythromycin Estolate**

Lilly

*(See next page for prescribing information.)*

# Ilosone®/the most active oral form of erythromycin

**Description:** Ilosone is the most active form of oral erythromycin that has been developed. Because it is stable in acid, well absorbed, and excreted in lesser amounts in the bile, it provides faster, higher, and longer-lasting levels of antibacterial activity (ABA) in the serum, even when taken with food, than do comparable doses of erythromycin.

**Indications:** Ilosone is indicated in infections caused by microorganisms sensitive to its action (especially staphylococci, hemolytic streptococci, and pneumococci). The drug is therefore useful in a high proportion of bacterial diseases encountered in clinical practice and particularly in the treatment of bacterial infections of the upper and lower respiratory tract and soft tissues.

In the treatment of acute bacterial pharyngitis and tonsillitis, this antibiotic has promptly eradicated the bacteria (streptococci) and has produced a parallel prompt clinical improvement. There have been no group A beta-hemolytic streptococci resistant to this preparation. In beta-hemolytic streptococcus infections, treatment should be maintained for ten days to prevent the development of rheumatic fever or glomerulonephritis.

Erythromycin estolate has proved to be very effective in pneumococcus pneumonia and in acute bronchitis with pneumococci on culture. Bronchopneumonia and otitis media in children have responded well to its use.

The antibiotic has been used very successfully in staphylococcus infections. Good therapeutic results have been obtained in soft-tissue infections, abscesses, cellulitis, carbuncles, wound infections, and furunculosis.

In serious staphylococcus infections, erythromycin preparations should be used only in combination therapy with other antimicrobial agents. As is the case with any treatment regimen used in these severe conditions, surgical procedures should be performed when indicated, and large dosages of the antimicrobial agents should be employed. In this fashion, Ilosone has been effective in staphylococcus pneumonia, osteomyelitis, septicemia, empyema, and meningitis.

Multiple 500-mg. doses of the drug have also been useful in gonorrhea and syphilis. Since penicillin is the drug of choice for the treatment of syphilis and gonorrhea, erythromycin estolate should be employed for these infections only in patients with a history of penicillin allergy. Also, other infections due to susceptible bacteria in patients known to be hypersensitive to penicillin or other antibiotics may be considered for treatment with Ilosone.

**Contraindications:** Ilosone is contraindicated in patients with a known history of sensitivity to this drug and in those with preexisting liver disease or dysfunction.

**Adverse Reactions:** Data obtained from seven years' use of propionyl erythromycin ester and erythromycin estolate (Ilosone) indicate that hepatic dysfunction with or without clinical jaundice may occur during or following courses of therapy with the drug.

Changes in liver function tests in such cases have been indicative of intrahepatic cholestasis. The symptoms appear to be the result of a form of sensitization. The initial symptoms have developed in some cases after a few days of treatment but generally have followed one or two weeks of continuous therapy or several courses of the drug. Symptoms reappear promptly, usually within forty-eight hours, if the drug is readministered to sensitive patients. Eosinophilia was noted in peripheral blood counts. The findings readily subsided without apparent residual effects when treatment was discontinued. Recovery was delayed in one reported instance. The physician indicated in this case that either drug-induced jaundice or viral hepatitis may have been responsible for the findings.

In one clinical study involving ninety-three patients treated with the antibiotic, three cases of jaundice were observed and an additional eleven cases developed some changes in liver function tests. Three of the patients had abnormal liver function tests a second time on readministration of the drug.

Even though it is assumed that not all cases of jaundice have been reported, it seems clear that the number is small compared with the amount of drug that has been used. Reported cases have included persons in whom there had been administered other drugs known to be associated at times with hepatic side-effects and cases in which the presence of viral hepatitis or other disease may have been responsible for the findings. In some of the cases, associated gastro-intestinal symptoms simulated the colic of biliary tract disease. In other instances, clinical symptoms and results of liver function tests resembled findings in extrahepatic obstructive jaundice. It appears that the occurrence of jaundice after administration of Ilosone is infrequent, but further investigations are being made to estimate its incidence more accurately.

In those cases mentioned above in which jaundice appeared
be definitely related to use of the drug, laboratory findings w
characterized by increased direct-reacting bilirubin, eleva
alkaline phosphatase levels, negative or weakly positive cepha
flocculation and thymol turbidity tests, elevated serum glutar
oxalacetic transaminase levels, peripheral eosinophilia, and n
mal cholecystograms.

Individual idiosyncrasy seems evident since jaundice has
been reported in other patients taking prolonged courses of
medication. Patients with chronic infection have been given 1
to 2 Gm. of the drug daily for periods of two to six months, a
patients with rheumatic fever have taken prophylactic doses
0.5 Gm. daily for two years without difficulty. In one group
144 patients who received the drug daily for two years, no jau
dice was noted. It was of interest that members of six of th
patients' families, who were not taking the drug, had episo
of jaundice during the study period.

Transaminase and serum alkaline phosphatase levels w
determined in a group of fifty-four adults and children who to
250 mg. of Ilosone daily for an average of sixteen months
rheumatic fever prophylaxis. The results were compared w
those of a similar group of forty-four patients who received pe
icillin. There were no cases of jaundice in either group. Elevati
of SGPT and serum alkaline phosphatase levels during the cou
of treatment was observed in one patient treated with Iloso
and in two patients treated with penicillin. Seven other patie
in the group receiving Ilosone and four others in the penicil
group showed elevations in one of the tests at some time duri
administration of the drugs.

Very satisfactory therapeutic results, without toxicity, we
reported in 102 pediatric patients who received short-term (te
day) courses of Ilosone in the treatment of streptococcus inf
tions. Results of liver function tests in these patients we
comparable to those in a similar control group who had receiv
penicillin.

Gastro-intestinal disturbances not associated with hepatic
fects are observed in a small proportion of individuals as a res
of a local stimulating effect of the medication on the alimenta
tract; however, the normal intestinal gram-negative bacteri
flora is not appreciably altered by erythromycin drugs.

Although allergic manifestations are uncommon with the u
of erythromycin, there have been occasional reports of urticari
skin eruptions, and, on rare occasions, anaphylaxis.

**Administration and Dosage:** Ilosone is administered orally.

Ilosone Pulvules®, Ilosone Liquid 125, Ilosone, 125, for Or
Suspension, Ilosone Drops, Ilosone Chewable Tablets.

For infants and for children under twenty-five pounds of bo
weight, the usual dosage is 5 mg. per pound every six hours; f
children twenty-five to fifty pounds, 125 mg. every six hou
(Tablets Ilosone Chewable should be chewed or crushed a
swallowed with water.)

For adults and for children over fifty pounds, the usual dosa
of Ilosone is 250 mg. every six hours.

For severe infections, these dosages may be doubled.

When larger doses are indicated, parenteral erythromyc
therapy should be considered.

In the treatment of syphilis, the recommended total dosage
20 to 30 Gm. given in divided doses for a period of ten to fifte
days. Close follow-up of the patient is necessary since erythr
mycin drugs have not had adequate evaluation in all stages
syphilis. Examinations of spinal fluid are recommended as pa
of the follow-up therapy.

For gonorrhea, 500 mg. four times a day for four days a
recommended. In the treatment of gonorrhea, patients with
suspected lesion of syphilis should have a dark-field examinati
before receiving antibiotics, and monthly serologic tests shou
be made for a period of three months.

**How Supplied:** Pulvules Ilosone, Capsules, N.F., 125 and 250 m
(equivalent to base), in bottles of 24 and 100.

Ilosone Liquid 125, Oral Suspension, U.S.P., 125 mg. (equivale
to base) per 5-cc. teaspoonful, in 60-cc. and pint-size package

Ilosone, 125, for Oral Suspension, N.F., 125 mg. (equivale
to base) per 5-cc. teaspoonful, in 60 and 150-cc.-size package

Ilosone Drops, 5 mg. (equivalent to base) per drop, in 10-cc.-si
packages, with dropper calibrated at 25 and 50 mg.

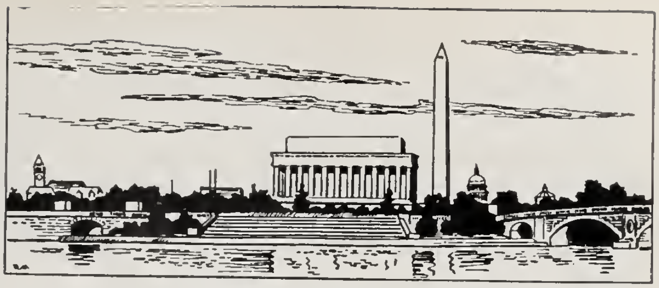
Tablets Ilosone Chewable, N.F., 125 mg. (equivalent to base
in bottles of 50. [03276

*References:* 1. Griffith, R. S., and Black, H. R.: Am. J. M. Sc., *247*:69, 196
2. Griffith, R. S., and Black, H. R.: Antibiotics & Chemother., *12*:398, 196
3. Hirsch. H. A., Pryles, C. V., and Finland, M.: Am. J. M. Sc., *239*:198, 1960.

*Additional information available to physicians upon request.*
*Eli Lilly and Company, Indianapolis, Indiana 46206.*

Lilly

700



# EDITORIALS

## The Progress of Medicine in The American Tropics

Over the years in the U.S.A. some of the most frequent questions asked of me pertain to disease instance, mortality rates, the progress of medicine, and the health and sanitation status of the people and countries as a whole in the Central and South American localities.

There is a prevailing feeling among those not in the know, so to speak, that the areas referred to are still plagued with serious diseases and that not a great deal of advancement has been made. This is untrue. There are numerous general hospitals and rural health centers scattered throughout the countries. They serve an excellent purpose and have improved health conditions remarkably during the past 15 years. In addition to this active step forward, good public health and preventive medicine programs are in progress.

I have spent many years in The Tropics. During the past 20 years considerable progress, as stated, has been made medicalwise in all directions in the tropical areas referred to. Now, in the most important sectors, health and sanitation are almost as good as in the U.S.A. Water is potable, milk is potable, sanitary standards are up appreciably, and most of the previously serious tropical diseases, such as malaria, yellow fever, filariasis, amoeba infections, typhoid fever, intestinal parasites, yaws, leishmaniasis, serious dysenteries, nutritional disturbances, and the like, are, practically speaking, a thing of the past. Also there is very little smallpox, tetanus, pertussis, diphtheria, poliomyelitis, and tuberculosis. Conditions now encountered by the physicians, for the most part, are the same as the run-of-the-mill in the U.S.A. Mortality rates have decreased appreciably, and the standard of medicine practiced by the average physician is good. There are still a few diseases, such as Chagas' disease, Venezuelan encephalitis, and arbovirus infirmities, peculiar to the regions, which are of interest to the researcher, but they are uncommon and cause no real serious problem.

The United Fruit Company has general hospitals, field hospitals, and dispensaries, scattered over Central America, which care for some 160,000 employees and dependents. All the facilities referred to are in rural areas. Below are some interesting statistics for the year 1966.

| | |
|---|---|
| Number of employees and their families | 161,000 |
| Number of outpatient visits | 968,484 |
| Number of patients admitted to hospitals | 31,000 |
| Number of hospital days | 153,700 |
| Average day-stay per patient in hospital (low) | 4.9 |
| Number of live births | 4,853 |
| Number of deaths | 406 |
| Death rate per 1,000 in our age group—live birth to 70 years (very low; U. S., around 7) | 2.5 |

To keep costs down, and they are very low for this number of eligibles, I have stressed: Do not admit to hospitals unless absolutely necessary; use outpatient treatment, where feasible; when admitted to hospital work up and treat fast, discharging as soon as possible. The latter is the reason for our very low average hospital day-stay per patient of 4.9 days.

In addition, the doctors are requested to think carefully before prescribing treatment, not to be wasteful in prescribing that which is not truly indicated nor that which might be harmful, and, lastly, not to order various diagnostic procedures unless there is a supporting reason. There was a tendency at one time to rely on all sorts of diagnostic procedures, often bypassing a good physical examination, in the attempt to establish a diagnosis. This has changed. It is also stressed that when something is indicated no corners are to be cut. Group ward rounds, medical library reading,

*Opinions expressed in contributions to the Editorial Section are those of the writers and do not necessarily reflect the views of the Medical Society of the District of Columbia*

medical conferences, medical discussion, etc. are emphasized.

Good preventive medicine, sanitation, and public health, as much as feasible, are promoted. Hence the forward progress which has been and is being made.

While some parts of the countries may not be as well along as our localities, much improvement has been made in general everywhere.

The foregoing should give some idea, to those not familiar with the situation, of advances which have been and are being made in the field of Medicine and Public Health in The American Tropics. Medical schools are also improving, as are those for training nurses.

L. M. Drennan, Jr., M.D.
*Medical Director, United Fruit Company*

## Policy on Use of Bank Credit Cards for Patients

Should you, as a physician, accept the use of your patient's bank credit cards as a means of paying or financing their medical bills?

The welfare of the patient is the main determinate in the decision. The indiscriminate use of the bank card system, especially in financing larger medical bills through banks, could result in additional cost to patients.

The AMA Judicial Council, in determining a general and uniform rule to guide the profession, recommends the following principles, to be implemented and applied as necessary by the county medical society for the guidance of physicians participating in bank card programs.

1. The county medical society should be satisfied as to the financial and professional integrity of the plan. It should negotiate with the plan sponsors to insure that service charges to the physician are reasonable. It should insist that the plan be open to all physicians on the same terms and that it not exploit or capitalize on physician's participation in the plan. It should advise the plan that the listing of physicians in directories of participating members is contrary to the ethics of the medical profession.

2. The individual physician may not, because of his participation, increase his fee for medical service rendered the patient. He may not use the plan to solicit patients. He may not encourage patients to use the plan. His position must be that he accepts the plan as a convenience to patients who desire to use it. Plaques or other devices indicating participation in the plan within the physician's office shall be kept to a discreet and dignified minimum. Plaques, signs, or other devices indicating such participation visible outside the physician's office are unacceptable.

3. The use of a bank card in connection with the payment of larger fees—which might normally be paid to the physician in installments—is not encouraged. All members of the Association are expected to continue the traditional practice of permitting patients of limited means to pay relatively large fees in installments without interest or carrying charges. Out of respect for the dignity and traditions of the medical profession, the physician may not relieve himself of his obligations "to render service to humanity, reward or financial gain being a subordinate consideration."

G. W. C.

**KEOGH RETIREMENT PLANS**

Individually Designed for Each Physician or
Partnership and Funded with Leading Mutual Funds
and Insurance Annuities in Major Companies

**EUGENE F. ROESSER, C.L.U.**

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District 7-1114

## Use and Misuse of Drugs

In the communication on page 425 there is a review of drug dependence classification and the Drug Abuse Control Amendments with which we should all be familiar, especially as they relate to stimulants and depressants. Some of the latter are termed "minor" tranquilizers, but in terms of drug dependence only, these minor tranquilizers are much more hazardous than the so-called major tranquilizers. All physicians realize that potent drugs have some untoward effects that vary from drug to drug and from patient to patient, but the potential for dependence needs to be emphasized with stimulants, sedatives, and minor tranquilizers, especially since this possibility was minimized when many of these drugs first appeared.

Apart from legal restrictions it would seem consistent with good medical practice to stay within the maximum of 5 refills for any prescription for a sedative or stimulant drug. Many times no refills are indicated. Additionally, it may often be a judicious preventive measure to warn patients explicitly that they should never take such medication more often or in greater amounts than that prescribed.

In the future it would be useful for physicians in this area to have a task force available to them to help exchange concerns, information, and ideas about drug dependence issues. This would facilitate a growth of the knowledge about the kinds and the amount of drug abuse in the Washington community. In line with this objective the Committee on Problems of Drug Dependence of the Washington Psychiatric Society will call attention in forthcoming issues of the Medical Annals to some of these issues. In the meantime the Committee would appreciate it if members of the D. C. Medical Society will comment on or relate their experiences concerning problems of drug abuse or misuse.

Committee on Problems of Drug Dependence
*Washington Psychiatric Society*

## Howard Symposium on Medicine and Law—A Brief Report

A symposium on law as it relates to medical practice was held at Howard University as a feature of the Annual Convention of the Student National Medical Association on Saturday, April 29, 1967. The principal speaker was Dr. Sidney Shindell, Professor of Medical Jurisprudence at Marquette University. His remarks were concerned with various aspects of medical malpractice, emphasizing that most malpractice suits have their origin in some careless remark made by another physician who subsequently saw the patient. He also noted that good patient-doctor relationship was very important to resolve possible malpractice suits, especially in cases in which treatment has not yielded optimum results or where there has been a collection problem or a source of irritation in the course of the patient's medical problem.

Other points developed in the symposium by Dr. J. Rogers Young, of Casualty Hospital, and Dr. Everett J. Gordon, of Georgetown University, involved the Good Samaritan Law and the management of medicolegal cases in actual practice. Dr. Young emphasized the necessity of giving first aid, when necessary, as a moral and ethical principle, and further noted that there has never been recorded any successful suit for malpractice against a physician for rendering first aid. Dr. Gordon pointed out the need for a comprehensive, impartial medical report based on an objective physical examination and X-rays as indicated.

The symposium concluded with a statement that a competent medical examination and impartial reports would result in most medicolegal cases being settled or fairly adjudicated at trial. Many of the students expressed interest in the subject by participating in a lively question-and-answer period which followed the formal presentation.

Everett J. Gordon, M.D.

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*60 years serving the medical profession*
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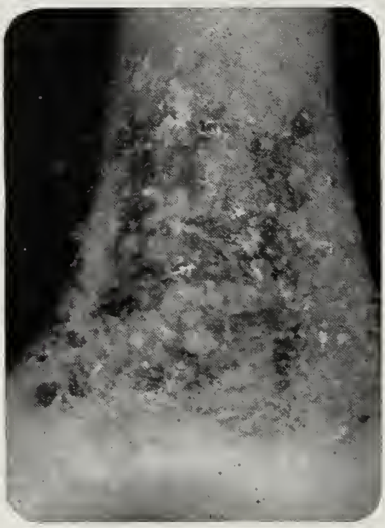
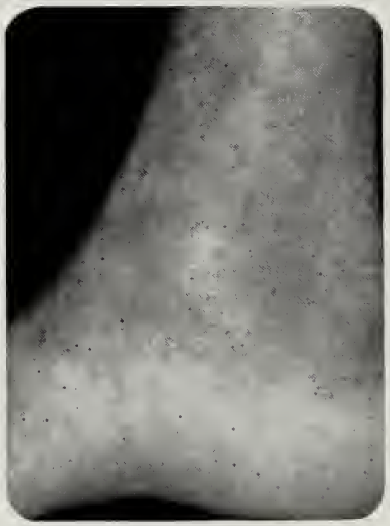
Federal 8-2688
Medical and Surgical Supplies
Hospital, Invalid and Sickroom Supplies
Surgical Fitting Specialists—Man and Woman
Private Fitting Rooms

**Eczema of many years...**
**controlled in two weeks**



*Before treatment*



*After treatment* —
with ARISTOCORT Topical
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*Administration and Dosage:* Apply sparingly to the affected area 3 or 4 times daily. Some cases of psoriasis may be more effectively treated if the 0.1% Cream or Ointment is applied under an occlusive dressing.

*Contraindications:* Tuberculosis of the skin, herpes simplex, chicken pox and vaccinia.

*Precautions and Side Effects:* Do not use in the eyes or in the ear (if drum is perforated). A few individuals react unfavorably under certain conditions. If side effects are encountered, the drug should be discontinued and appropriate measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive nonpermeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyodermas will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

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406-6

# Question of the Month—?

**With the potential of "free choice" medical care for the indigent of the District of Columbia and with prepayment plans draining away teaching cases, can private patients fulfill the needs for intern-resident teaching programs?**

### Answers and Comments

THOMAS E. CURTIN, M.D. (Internal Medicine): The answer is they must. Participation in patient care is necessary in training. This includes increasing responsibility for the trainee under supervision of attending physicians. The patient is vital to this concept.

At present all teaching hospitals consider every patient as a teaching case. It is so stated either in the Constitution and By-laws or in the agreement when a physician receives privileges at a hospital.

The surgical specialties will have a more serious problem than the medical. A patient's agreement to a trainee performing his surgery will have to be established. Details of this problem have not been solved. Several ideas have been proposed but to my knowledge an official solution is still forthcoming; but it must come. Patients, private or otherwise, must fulfill their role in the training of young physicians. This system has proven its worth; I cannot conceive of any other.

JAMES R. SNYDER, M.D. (Internal Medicine): The answer is yes. The medical profession, responsive to the demands of an informed and restless society, is critically evaluating its education system. It is apparent that graduate education must develop in an environment similar to what we now appreciate as private practice.

It would be discouraging to consider graduate medical training to be dependent upon an indigent population unable to select a particular physician.

The house officer expects, and should have, a comprehensive training program. In the portion directed toward bedside teaching it necessitates his direct involvement in patient management.

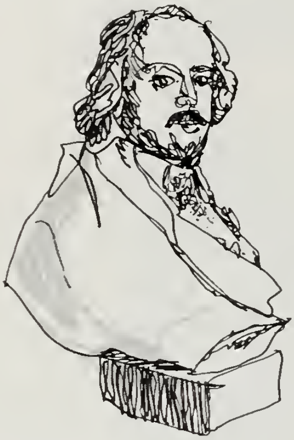
We have developed an approved education program with a private patient population. The resident under the direct supervision of the attending physician, directs the patient's diagnostic and therapeutic programs, while being readily available to attend to the medical problems involved.

It is important to note that no difficulties have occurred in demonstrating interesting patients. In fact, when compared to their indigent counterpart private patients are more responsive and coöperative and consequently effective for teaching purposes.

JOHN A. KENNEY, JR., M.D. (Dermatology): The answer is yes. I believe private patients can fill the need for intern-resident teaching programs if we will all adopt the philosophy (and make our hospital regulations conform to it) that all patients are potential teaching patients. There has too long been an artificial distinction between the "clinic" patient and the "paying" patient. With the anticipated shortage of "clinic" patients, we shall have to bring interns and residents in on our private cases, i.e., to examine and treat patients under our supervision, to a much greater extent than has been true in the past. Our training programs are most essential and we must see to it that all patients are utilized for teaching in accordance with the special educational aspects which each case presents.

JAMES A. CURTIN, M.D. (Internal Medicine): Private patients are participating in the graduate education programs of physicians in many hospitals. It is essential that these programs not only continue but become stronger. It is necessary that the patients be made aware of the advantages of having house staff participation in their care. Most patients would probably prefer this type care under a team headed by their physician or surgeon.

Some departments divide the services into a Teaching Service (the house staff participates in the care) and a Nonteaching Service (the total care is by the attending) and house staff are not assigned. Patients could then choose to be assigned to the Nonteaching Service. If the patient is informed and makes a choice there should be no cause for later misunderstanding. The attending would have to decide too if he wished to accept responsibility for patient care under such circumstances.



*Adaptation from Shakespeare Rare Print Collection*

*"Give me a bowl of wine*
*—in this I bury*
*all unkindness"*

—SHAKESPEARE

**DEAR DOCTOR:**

Will Shakespeare was a pretty fair hostler and real estate investor, a pal of Francis Drake and Walter Raleigh, much admired by Queen Elizabeth, and a tophole poet and playwright —but no physician.

Nevertheless, he had a rather good idea of the helpfulness of wine in cases of stress, as you can see above.

Like Will, we wish to recommend a daily bit of wine, with your meals for your own personal stress, Doctor, in your rugged profession.

Also, for your wife's stress at home, we'd like to prescribe a 24-page folder, "WINE COOKERY THE EASY WAY," which will help her to relax in the kitchen (and help you at the barbecue). We'll mail it to you (free) if you'll just drop us a note on your professional letterhead.

By the way, we'll also send you our newly revised 64-page booklet, "USES OF WINE IN MEDICAL PRACTICE," which summarizes a quarter century of scientific research, in America and Europe, as an aid to your profession.

We hope you will request one or both of these free booklets.

As you know, wine stimulates gastric flow; can help the convalescing patient; the patient lacking appetite; can help relieve anxiety; can help patients suffering from the malabsorption syndrome—and helps hospital and geriatric home morale. Shakespeare had a good idea there. And many physicians and hospital administrators are also sharing that idea.

Here's a toast in California wine, Doctor—to your health!

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# Stimulant and Depressant Dependence: Drug Abuse Control Amendments*

DOROTHY S. DOBBS, M.D.†, AND ROGER PEELE, M.D.‡

TWO DEVELOPMENTS in the past 3 years have contributed to a second look at drug abuse: (1) change in classification, and (2) the Drug Abuse Control Amendments. We are briefly summarizing these and presenting an overview of clinical experience with stimulants and depressants.

### Classification Change

Classification by the terms "addiction" and "habituation" led to an unintended conceptual hierarchy as to the severity of the problem. There was some risk that arbitrary categorization determined the dangerousness of a drug and in turn the severity of a patient's problem with drugs. In order to avoid rigidity and provide a classification that could easily accommodate new findings, world and national organizations concerned with drug use, misuse, and abuse have advocated a newer classification centered around the term "dependence." Drug dependence is conceived of as "a state of psychic or physical dependence, or both, on a drug arising in a person following administration of that drug on a periodic or continuous basis. The characterization of such a state will vary with the agent involved, and these characteristics must always be made clear by designating the particular type of drug dependence in each specific case; for example, drug dependence of the morphine type, of the barbiturate type, of the amphetamine type, et cetera. . . ."[1]

### Amphetamines

Continual overuse of stimulants may produce increased signs of sympathetic activity, apprehension, combativeness, or marked reduction of critical self-evaluation. Later, sullenness, anger, and suspiciousness may appear, and these aberrations can develop further into delusions, hallucinations, panic, and confusion. Tolerance is considerable in some cases, with reports of an intake of over 1,000 mg. a day before the appearance of clinical signs.[2] Although oral administration is more common in the D. C. area, intravenous use has occasionally been reported.

Lemere[3] has cited Japanese workers who have reported that prolonged overuse of amphetamines can cause irreversible brain damage resulting in decreased intellectual functioning and lethargy. Others believe that a permanent personality change may take place.[4] Since our experience has been limited to seeing patients after they have become amphetamine-dependent, the change is difficult to determine; however, we do know of 1 patient who stated that he had episodes of very poor concentration even though he had been off amphetamines for 15 months.

In another case, Mr. A., a 40-year-old shop foreman, was hospitalized after acting on bizarre delusions. He had stopped school after the sixth grade and was a delinquent in his teens. After World War II he was swiftly promoted many times by a unit known for making severe demands on its employees. His domestic situation was unusual. He was supporting the children of a lady he had divorced in the 1940's, his second wife and her children, and a common-law wife and her children. A typical evening saw him come home to one family and have dinner, then depart "to go to work" and see the other family. Both women, but not the children, were aware of the situation. Besides supporting 3 sets of children, supporting 2 wives, and often working overtime as a foreman, he participated in union activities. One morning he tried the "diet pills" (amphetamines) of one of his wives and soon felt these were what he needed to "get over the hump" and began taking them regularly. After several years of increasing the dosage gradually, a delusional system began to develop leading to hospitalization.

Persons dependent on amphetamines approach doctors complaining of fatigue, sadness, or obesity. Obesity does not rule out the possibility that patients have been overusers of amphetamines for years. Some of our overusers remained obese while taking amphetamines. Certainly, dependence is to be suspected when a patient pressing for continuation of amphetamine is not losing weight.

Treatment of the brain syndrome nearly always requires hospitalization to stop the use of drugs and sometimes is required to prevent homicide or suicide. There are no physical withdrawal phenomena per se, no specific drug for withdrawal, and no immediate therapy for the symptoms. The treatment of the dependence involves education regarding the dangers, psychotherapy for any underlying problems, and support to enable the patient to reach goals without the extra "help" that the drugs provide. An undetermined percentage of patients, usually those taking only 2 to 4 times the prescribed dose, will stop when their physicians demand that they do.[4] If this fails and the patient has a second episode, the outlook is less good, and a fully effective approach has yet to be established.

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* The views expressed in this paper are those of the authors and do not necessarily reflect those of the institutions with which they are associated.

† Staff member, Saint Elizabeths Hospital, Washington, D. C. 20032.

‡ Staff member, Saint Elizabeths Hospital; Assistant Clinical Professor of Psychiatry, George Washington University School of Medicine.

### Sedatives and Minor Tranquilizers

This group of agents will be discussed together because of similar signs, symptoms, and treatment of states of dependence. Overuse of drugs such as barbiturates, chlordiazepoxide (Librium®), diazepam (Valium®), ethchlorvynol (Placidyl®), glutethimide (Doriden®), meprobamate (Equanil®, Miltown®), and methyprylon (Noludar®) can cause toxic effects of ataxia, slurred speech, and confusion. The abstinence-syndrome consists of convulsions, confusion, hallucinations, and muscle twitching or tremors. Evaluation is not easy because the patient may look and feel fine many hours after his last dose, yet the diagnosis cannot be postponed because treatment must be instituted promptly if serious problems associated with physical dependence are to be avoided.

Mr. B., a 50-year-old executive, was admitted to a local hospital after suffering his initial convulsion while on the way home from work. He had left work in mid-afternoon because he was "jumpy," his muscles were sore, and he felt hot. After some reluctance he gave a history of heavy drinking in his twenties. During his thirties he began drinking on the job, was in danger of being discovered, and switched to barbiturates. During his days off he visited doctors, complained of having trouble getting to sleep, and often received prescriptions for substantial amounts of barbiturates. A routine day consisted of 2 to 4 capsules in the morning, 2 to 4 in the afternoon, a few after dinner, and 4 to 8 to help him sleep. He slept with a jar of instant coffee under his pillow, and after the alarm went off he would eat the instant coffee by the spoonful until "fully" awake. After the Drug Abuse Control Amendments were enacted in 1965, even before their implementation in 1966, he found it much harder to obtain prescriptions from physicians. On the afternoon of admission he had had no drugs since the previous night. He believed he could get barbiturates illicitly but, because of his conscience, was "compelled to take only what doctors had sanctioned."

Mrs. C., a 37-year-old housewife with 3 children, was initially seen in the late 1950's complaining of difficulty in concentrating, fatigue, insomnia, and of being constantly irritated with her children. She was placed on meprobamate and was told by her psychiatrist that it was relatively safe and not "addictive." She gradually increased the dosage until she was taking 2 to 4 times the prescribed 1,600 mg. daily. Subsequently, she had much greater difficulty obtaining a constant supply, with days when she received less than she wanted, felt panicky, could not sleep, and would drink enough liquor to become stuporous. The increased drinking and the irregular dose of meprobamate kept her vacillating between a dizzy or ataxic state and that of apprehension or irritability (intoxication and withdrawal). A general practitioner recognized the difficulty, refused to continue prescribing meprobamate, and recommended that she be hospitalized. Hospitalization she would agree to, but not if it meant no more meprobamate, which "I can't live without." She moved to another community and found a source of meprobamate. Her present approach toward handling her irritation with her children is to give them meprobamate too!

It is often stressed that a person dependent on one substance is prone to be dependent on other substances. A striking example was Mr. D., a 38-year-old drug salesman, who had a 15-year history of drug and alcoholic overuse. After losing his job and family and being hospitalized frequently, he finally managed to do without drugs and alcohol for several years. Then he received some chlordiazepoxide for reduction of evening tension in order that he could get to sleep. He took 20 mg. the first evening and felt it helped a little. The next night he decided that 40 mg. would help more, and the third night he took approximately 100 mg. After that he lost count and was hospitalized in a very confused state less than a week after the initial 20 mg. dose.

Evaluation and treatment of persons dependent on sedatives or minor tranquilizers can be the same in either case. An established approach is to administer a test dose of 200 mg. of pentobarbital; if the patient is not sedated, tolerance is demonstrated. The patient should then be hospitalized and stabilized on pentobarbital, and then pentobarbital should be administered in gradually decreasing dosage. This method has been described in detail by Ewing and Bakewell[5] and Essig.[6]

## The Drug Abuse Control Amendments

Increasing concern over problems of non-narcotic drug abuse led to Federal legislation in this field. Enacted in July 1965, the Drug Abuse Control Amendments became effective February 1, 1966. The law specifically designated barbiturates, amphetamines, and the hallucinogens (available only for investigational use) as subject to controls. Other drugs which are central nervous system depressants or stimulants and which have been found to have a potential for abuse have also been controlled. These are:

Depressants:
- Chloral betaine (Beta-Chlor®)
- Chloral hydrate (Chloral®)
- Chlorhexadol (Lora®)
- Ethchlorvynol (Placidyl®)
- Ethinamate (Valmid®)
- Glutethimide (Doriden®)
- Methyprylon (Noludar®)
- Paraldehyde
- Petrichloral (Periclor®)
- Sulfondiethylmethane (Tetronal®)
- Sulfonethylmethane (Trional®)
- Sulfonmethane (Sulfonal®)

Stimulants:
- d-,dl-methamphetamine
- (d-,dl-desoxyephedrine) and their salts
- Phenmetrazine (Preludin®)

Pending the final outcome of hearings on meprobamate (Miltown, Equanil), chlordiazepoxide (Librium), and diazepam (Valium), these drugs are not presently subject to controls.

Although the primary target of this Act of Congress is the illicit drug traffic, certain provisions are of interest to the prescribing physician. For the controlled drugs no prescriptions older than 6 months can be filled nor can refills be made more than 5 times. This safeguard interferes minimally if at all with the physician's administration of generally useful drugs for patients whose symptoms are appropriately relieved by them. This limitation may, however, serve as an alerting signal to the physician that problems of tolerance and drug dependence (physical, psychologic, or both) may arise in association with any of the designated agents.

Other provisions of the Act require that manufacturers, wholesale druggists, pharmacists, hospitals, clinics, and certain other facilities keep accurate records on the controlled drugs. Record-keeping requirements apply only to those physicians who regularly dispense (as distinguished from prescribing) the drugs. Enforcement rests with the Bureau of Drug Abuse Control of the Food and Drug Administration in coöperation with local authorities.

## Magnitude of the Problem

Two university psychiatric units report that approximately 1 in 14 patients admitted have a drug-dependence problem, in most instances involving sedatives, stimulants, or minor tranquilizers.[5,7] Nearly half of the patients combined several medications or combined a drug with alcohol. Clinically these mixtures are important to keep in mind. For example, a patient with a history of amphetamine dependence may be taking Dexamyl® (dextroamphetamine and amobarbital) in such amounts that convulsions from barbiturate withdrawal must be considered possible.

## Conclusion

Sedatives, stimulants, and minor tranquilizers are among those groups of drugs that are very frequently prescribed. Yet, in our summary of clinical experiences it is clear that toxicity, withdrawal, and dependence on these drugs are of major concern. Serious consequences of drug misuse and abuse have sometimes been hidden behind the terms "nonaddictive" and "nonbarbiturate." The changes in medical classification and the Drug Abuse Control Amendments will help keep us aware of the profound harm that the therapeutically useful sedatives, stimulants, and minor tranquilizers can cause some of our patients.

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# Health Dept. Notes

### Health Planning Legislation

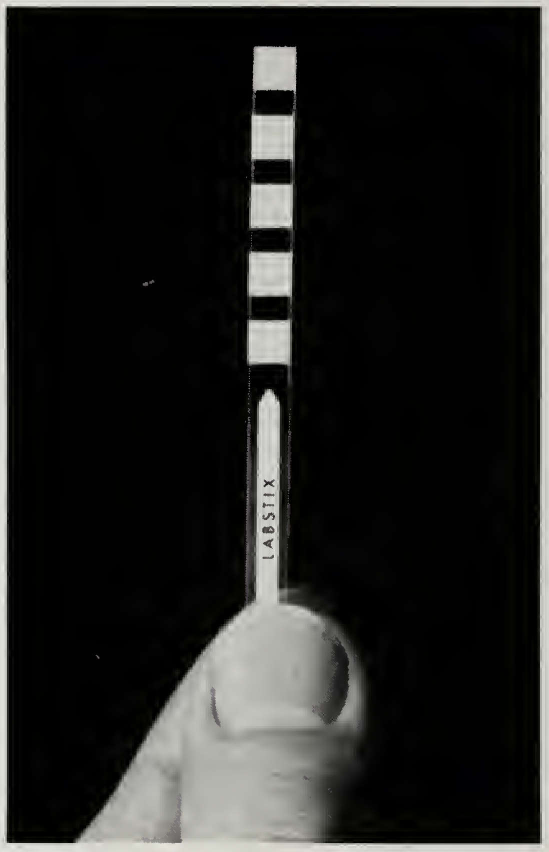
LEGISLATION passed by the 89th Congress will affect the health services provided in the District of Columbia. Public Law 89–749, known as the "Comprehensive Health Planning and Public Health Services Amendments of 1966," provides opportunities for community health planning in order to assure high quality comprehensive health services for all.

In passing the legislation members of Congress recognized the need for an effective partnership between Federal, state and local governments and voluntary health agencies for promoting health. Federal financial assistance will be available to assure comprehensive health services for every person but without interference with existing patterns of private medical practice.

In the District of Columbia the D. C. Department of Public Health has been designated the State Health Planning Agency. It is expected that the Public Health Advisory Council will serve as the State Health Planning Council in D. C. The Council, with membership from local health agencies, must include consumers of health services and will be required to advise the State Agency in carrying out its function under this plan.

The D. C. State Health Planning Agency will not replace existing planning mechanisms in specialized programs, such as hospital and other health facilities, construction programs, mental retardation programs, or construction of community health centers. Rather, the Act is designed "to help bring order into the statewide health planning process." The Act provides resources to measure and evaluate special health needs of each of the states and would make it possible to establish priorities for meeting these needs.

There are several major provisions of this law which will affect the District. One provision makes funds available for comprehensive planning, while another makes funds available for area-wide planning. Because of the District's proximity to Maryland and Virginia, area-wide planning will play an important role in District programs. Some areas of coöperation could include plans for emergency rooms, ambulance service, health information, environmental health, heart, cancer, and other disease control activities.



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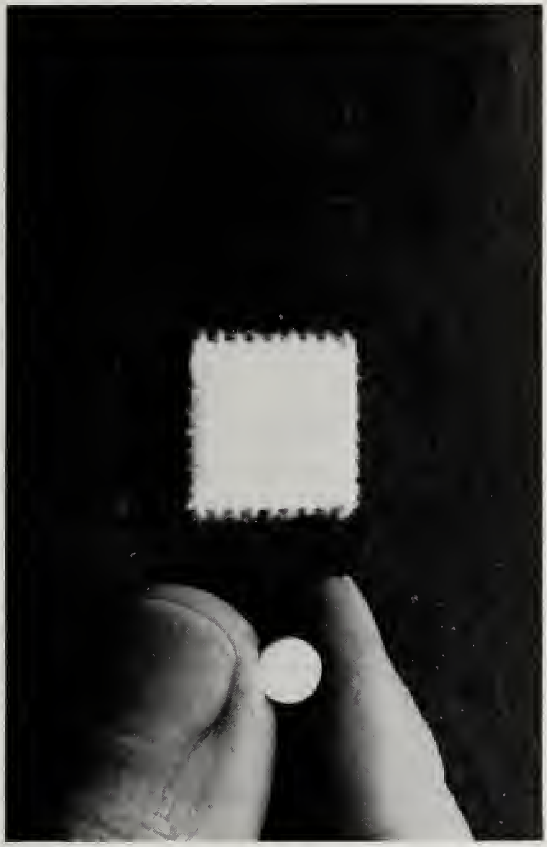

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A third section of the law eliminates categorical disease-oriented grants and substitutes a "block grant" which can be apportioned at the state level to meet the most pressing health needs. These needs will be determined locally.

During the past several months the D. C. Department of Public Health has given careful thought about carrying out plans for programs to improve the health of District residents. Although the funds to support these activities have not been appropriated, we are attempting to make an appraisal of the impact of the legislation on the existing organizations and programs of the Department and community.

The Act provides for flexibility in planning the types and quantity of resources needed most to serve the health needs of the people in our community as well as an opportunity to develop programs to find new or better methods of organizing and delivering personnel and environmental health services.

MURRAY GRANT, M.D., D.P.H.
*D. C. Director of Public Health*

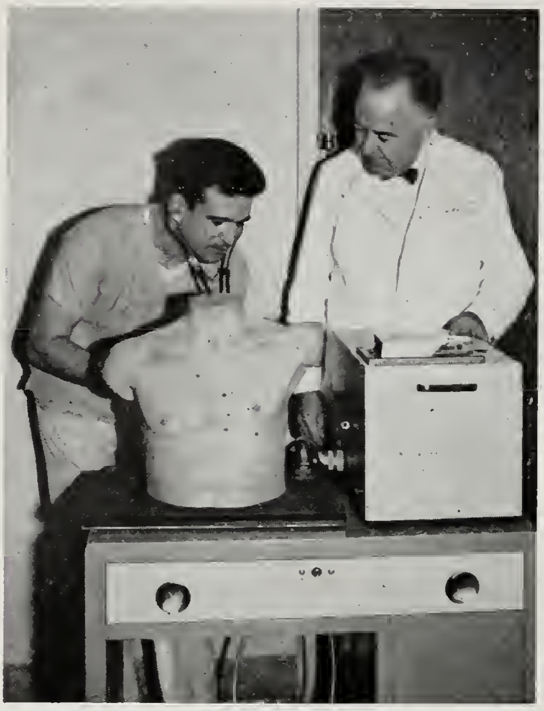
# DOCPAC Briefs

## or
## If You're Not "Political" You Should Be

RECENTLY a colleague of mine who, I am sure, is representative of many physicians belonging to the Medical Society of the District of Columbia, was complaining quite vociferously about the recent tax increases both local and national. He felt that he is "quite put upon" by the tax burden that he is compelled to carry.

I immediately asked him if he was a member of DOCPAC, the nonpartisan political action movement of the physicians of the District of Columbia. His answer was, "I am not very political."

This colleague may not consider himself "very political" but he is certainly quite political when it comes to complaining about his taxes. Good government is important to all physicians, and no physician should remain silent when that function or his profession is threatened. It is the individual responsibility of all of us, through our professional and civic organizations, to try to elect the best qualified men to office and through these men to aid in the passage of bills that help



**TERRY THE TORSO:** Dr. Thomas M. Peery (right), Professor and Chairman of the Department of Pathology at George Washington University, displays his teaching mannikin and how it works to medical student Jose Fabrega.

The National Fund for Medical Education provided the grant that enabled Terry to be developed. Dr. Peery worked with professors from GWU School of Engineering and Applied Science on the design of electronic components that would have to be incorporated in the torso. Electronics for the sound system were designed by Cooke Engineering Company of Alexandria, Va., and the sculpture for the torso was done by the Richard Rush Studio of Chicago.

Medical students in the basic class of physical diagnosis can use their stethoscopes on Terry to hear sounds that correspond to those areas where the 4 heart valves are best heard or to 4 strategic positions over the lung fields.

improve our government at all levels. This is the reason to join DOCPAC, an arm of the American Medical Political Action Committee. As stated before, AMPAC and DOCPAC wear no party labels. We support candidates entirely on the basis of what they stand for and we support candidates from both political parties. AMPAC is not a one-shot organization but a permanent group with the 2-fold purpose of providing reliable information to its members on political matters and working effectively to support good candidates. AMPAC and DOCPAC are not seeking to replace similar groups working in the individual states or in the District of Columbia but rather to supplement them.

Whether you feel you are political or not, you owe it to your local government, your national government, and to yourself to join DOCPAC now, and through DOCPAC, AMPAC. Individual dues are $20.00 a year, family dues $30.00 a year, and contributions are accepted up to $99.99. Write DOCPAC, 825 New Hampshire Avenue, N.W., Washington, D. C. 20037.

William H. Cooper, M.D.
*Chairman, District of Columbia*
*Political Action Committee*

## Health Problems in Education

Eight resolutions were adopted by the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association at its Annual Meeting in Chicago, February 26, 27 and 28.

Briefly stated, the resolutions were:

*Local Implementation of Federal Legislation:* That local agencies preparing guidelines for education legislation involve the medical, dental, nursing and allied health professions in planning implementation of programs, and that state and local medical societies contact the appropriate educational authorities or other responsible agencies with respect to implementation involving health components.

*Misuse of Drugs:* That the dangers of misusing and the advantages of correctly using drugs should be taught to all children, and that such education should be a continuing important part of the total curriculum of health education.

*Professional Preparation of All Teachers and Administrators:* That it be a requirement that all prospective teachers and administrators participate in professional courses of health education to qualify for recommendation for certification, and that in-service training programs be offered in the various school districts to supplement and update the education of teachers and administrators currently in the profession.

*Continued Venereal Disease Education:* That all physicians, public health personnel, and other agencies involved in health education continue their efforts toward venereal disease eradication, and that schools, particularly, continue to pursue a vigorous program of venereal disease education as a part of communicable disease instruction in the health education curriculum.

*Time for Health Instruction:* That further experimentation in curriculum development and design be carried out with emphasis on innovation in terms of inclusion of direct teaching of health in the curriculum, and that those school administrators who have provided through ingenuity and innovation appropriate time for teaching health be commended for their efforts to assure young people, in our schools, the health instruction they need and dserve.

*Balanced Curriculum:* That schools be encouraged to be flexible enough to meet the current needs of our times, and that schools make every effort to teach all important aspects of health with the proper emphasis and to discourage an overemphasis on popular problems at the expense of a total balanced health education program for children and youth.

*Measles (Rubeola) Eradication:* That the Joint Committee strongly support the measles eradication programs currently being sponsored by the American Medical Association and the Public Health Service of the United States Department of Health, Education, and Welfare, and that both parent organizations urge each of its members—physicians, educators, and others—to join with local medical, health and education agencies in a vigorous campaign to eradicate measles throughout the United States.

*Consumer Education:* That the Joint Committee on Health Problems in Education reaffirm its 1964 Resolution on Consumer Education, and that this resolution be widely disseminated through all appropriate channels.

The 1964 resolution referred to had 4-fold objectives:

1. That the schools in every community incorporate appropriate units on consumer education into their health education programs.
2. That competency in critical analysis of advertising and ability to discriminate between qualified and unqualified health personnel be the goal of such instruction.
3. That the American Medical Association and the Food and Drug Administration continue to sponsor periodic conferences on Quackery and Health.
4. That the resource units currently being developed under the sponsorship of the American Medical Association on consumer education and health be widely distributed and utilized in the Nation's schools.

## Dr. Kurtz Reëlected Head of Cancer Society

Dr. C. Roger Kurtz was reëlected President of the American Cancer Society, District of Columbia Division, May 18, by the Society's Board of Trustees, following the 20th Anniversary Meeting of the Society in the D. C. Medical Society Building.

A highlight of the meeting was the premiere showing of the Cancer Society's supported film, "To Speak Again," narrated by Arthur Godfrey and presented by David M. Resnick, Ph.D., Director, Hearing and Speech Center, Washington Hospital Center.

The St. George Medal and Citation for outstanding contributions to cancer control went to Mr. Leonard J. Emmerglick, Past President of the Division and a member of the Society's Executive Committee.

Dr. J. Keith Cromer was recognized for having served in the cause of cancer control for more than 10 years.

Four physicians received Certificates of Appreciation for conducting 25 or more of the cancer educational programs for the general public. They were Drs. S. Joseph Cosimano, Jr., Orville W. Donnelly, Lois I. Platt, and Warren J. Strudwick.

Dr. Jerome W. Canter was one of the 8 newly elected members of the Board of Trustees of the Society. Among those reëlected to the Board were Drs. Kurtz, K. Albert Harden, Stafford W. Hawken, Joseph W. Peabody, Jr., John F. Potter, John C. Rose, James G. Sites, and Jack E. White.

At the organizational meeting of the Board 17 persons were named to the Society's Executive Committee in addition to the officers. Included were the following members of the D. C. Medical Society: Drs. Cosimano, Sites, Edward E. Ferguson, Robert S. Jason, Calvin T. Klopp, LaSalle D. Leffall, Jr., and Cyril A. Schulman. Dr. Klopp was elected professional Delegate to the Society's National Office.

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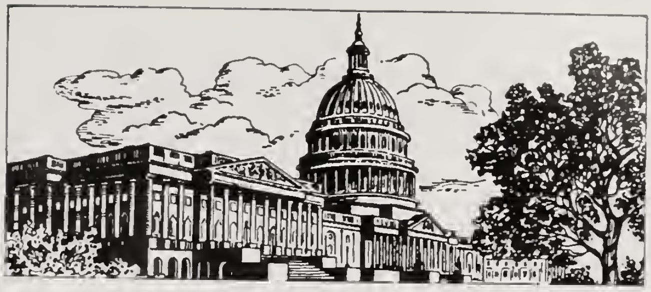


# NEWS & PERSONALS

## Summary of Executive Board Actions

### Proceedings of April 24 Meeting

Dinner for the Board members was served at 6:30 p.m. in the Exhibit Hall of the Medical Society. Dr. Karl C. Corley, Chairman, presided at the meeting. Present were Drs. Frank S. Bacon, C. Willard Camalier, Jr., Henry D. Ecker, Raymond T. Holden, Margaret M. Kenrick, Edward W. Nicklas, and Mr. George W. Cooley, Secretary. The meeting was called to order at 7:10 p.m.

The minutes of the April 3, 1967 meeting were approved as mailed.

**Committee Meetings:** The Secretary reported the following committees had met since the last meeting of the Board:

April 5 Fee Review Committee
6 Committee on Liaison with the Department of Motor Vehicles
6 Subcommittee on Environmental Health
7 Committee on Child Welfare
11 Committe on Medicolegal Problems
11 Membership Committee
12 Committee on Regional Medical Programs
12 Health Foundation of D. C.
14 Hospital Utilization Committee
18 Grievance Committee
19 Board of Credentials

**Board of Credentials:** The following actions were taken on recommendations made by the Board of Credentials:

*Active Members*

Charles P. H. Carroll, 730 24th Street, N.W.
Frederick Peter Litwin, 110 Irving Street, N.W.
Thomas M. Mould, 3000 Connecticut Avenue, N.W.
Irwin Shuman, 916 19th Street, N.W.
James Thomas Williams, Freedmen's Hospital

*Associate Members*

Alfredo de Jesus Dias, Suburban Hospital, Bethesda, Md.
Mohamed Y. A. Heshmat, 402 Chillum Road, Hyattsville, Md.

*Transfers*

*Associate to Life:* Cecile L. Fusfeld
*Associate to Active:* Socorro Abela-Palmon, Yussef Akbari, Recep Ari, Peter H. Bulle, Alexander M. Burnett, Jae Hyung Choi, Antonio C. deLeon, Jr., Oshin Der-Stepanian, Ai Ding Fang, William B. Glew, Hugo F. Keunen, John G. Lofft, Peter C. Luchsinger, Guilford E. Naranjit, Ali R. Sarioglu, Hans H. Schneider, and Jo Shibuya.
*Resident-Intern to Active:* Peter Oberhoff

*Resignations*

*Associate:* Roland E. Bieren and Morrill C. Quinnam, Jr.
*Resident-Intern:* Leon Rand

**Annual Financial Audit:** A motion was made and carried to accept the Secretary-Treasurer's statement on income and expenses for 1966 and the budget for 1967.

**AMPAC and DOCPAC:** Representatives of these organizations had been invited to attend this meeting of the Board and Dr. William H. Cooper, Chairman of DOCPAC, introduced the other guests: Dr. Frank C. Coleman, of Tampa, Fla., Chairman of the Board of Trustees of AMPAC; Mrs. Ann Rapee, Dr. Richard T. Sullivan, and Dr. Robert S. Poole, of the local DOCPAC organization; and Mr. William L. Watson, of Lemoyne, Pa., regional representative of AMPAC.

Dr. Coleman outlined the purposes of AMPAC and reviewed some of the successes that AMPAC had had during the last election year.

Dr. Coleman pointed out that any Medical Society (or AMA) contribution toward political action committees must be used for "housekeeping" and educational purposes and that all political contributions to candidates must come from individuals. He pointed out that 38 states have joint billing which include AMPAC dues on a voluntary basis and that it is in these states that they have had the greatest success in obtaining members. He felt that the legal advice that AMPAC has had concerning participation by Medical Societies was sound and that joint billing or other "housekeeping" or educational activities could be financed in part with Society contributions, including contributions in personnel, space, etc.

Dr. Cooper requested that the Executive Board consider including a separate bill (voluntary contribution) for DOCPAC in the Society's mailing of AMA dues for 1968.

Following a discussion period Dr. Cooper, Dr. Coleman and the other guests were thanked for appearing before the Board and excused.

The Board agreed in principle that physicians should interest themselves in political affairs and become active and participate as individuals. It was further agreed that DOCPAC be offered space in the MEDICAL ANNALS for the purpose of interesting physicians in joining the organization.

**Appointments to Projects Staff, Regional Medical Program of Metropolitan Washington (P. L. 89-239):** The Secretary reported on the Project Directors and Associate Project Directors selected by Dr. Desmond S. O'Doherty, Dr. Thomas W. Mattingly, and President Ecker. Eight of the 12 to be selected have now been named and are:

HEART: Project Director—Dr. Jack Segal; Associate Project Directors—Dr. Juan B. Calatayud (George Washington) and Dr. W. Proctor Harvey (Georgetown).

CANCER: Project Director—Dr. John Heller; Associate Project Directors—Dr. T. Crandall Alford (George Washington) and Dr. John F. Potter (Georgetown).

STROKE: Project Director—Dr. Warren V. Huber; Associate Project Director—Dr. Archie McPherson (Georgetown).

## Other Business

1. The President read a letter addressed to the Chairman of the Board from Dr. Preston A. McLendon suggesting that the Executive Board recommend Dr. Montague Cobb for appointment to the Board of Education of the District of Columbia. A motion was carried that a letter be written to Judge George L. Hart of the District Court supporting Dr. Cobb for appointment to the Board of Education.

2. The Secretary reported that the District of Columbia Interagency Council on Smoking had requested the Executive Board to support its request for a third grant of $36,367.65 for the period November 1, 1967 to October 31, 1968. The Secretary pointed out that the Executive Board assisted in the creation of the Interagency Council on Smoking and reviewed briefly some of its activities. The Board agreed to support the request for a third grant and to write such letters as necessary.

3. Election of AMA officers: As in the past, the delegates were instructed to use their best judgement at the Annual Meeting of the AMA in selecting those nominees to be supported.

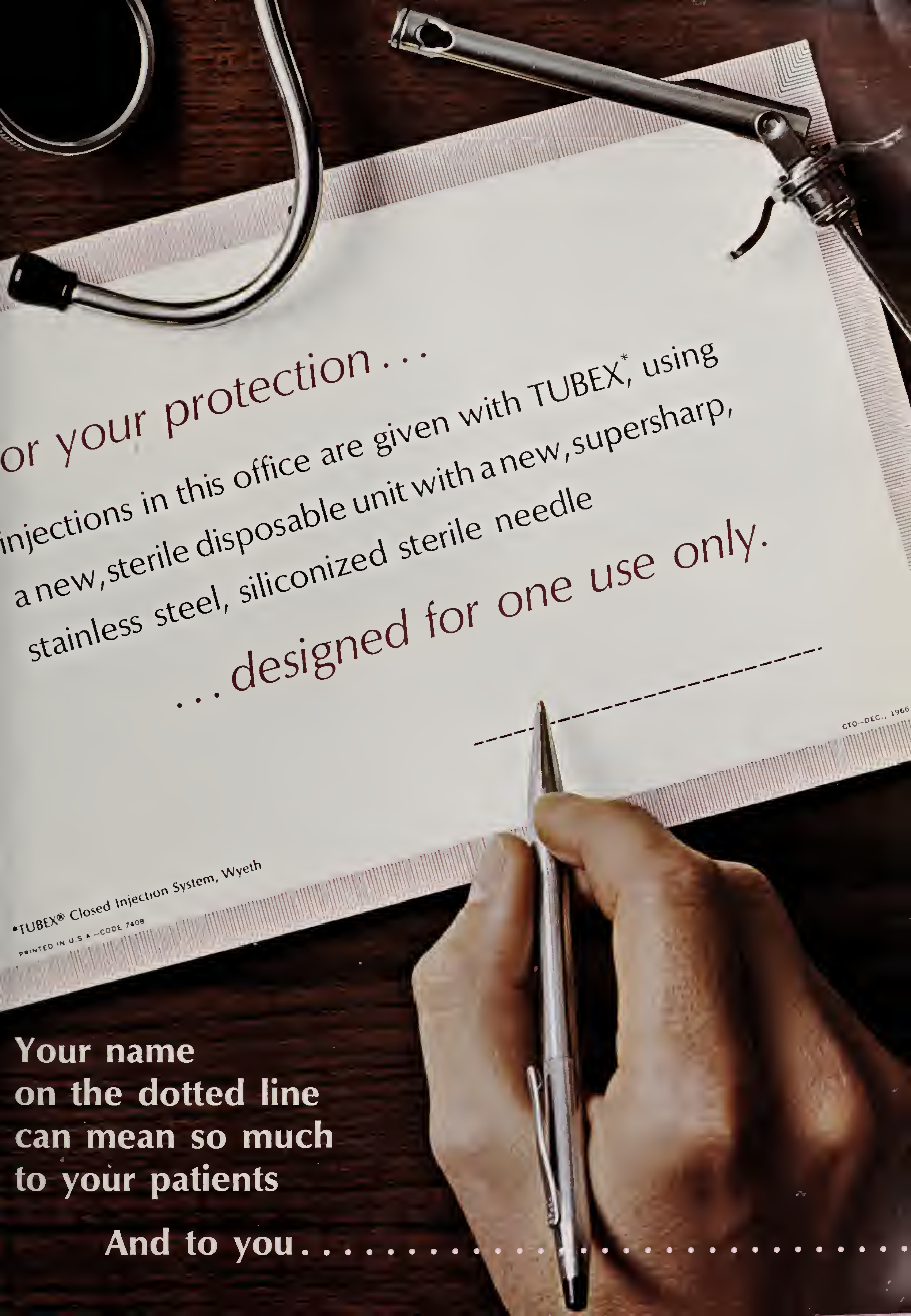
4. The Secretary reported on activities undertaken in reference to Dr. Murray Grant's efforts to amend the medical licensure law so that physicians working for the District of Columbia need not be licensed.

5. Telephone network on drug reactions: Dr. Ecker reviewed a request from Dr. James Long of F.D.A. to meet with Society representatives in regard to using the District as a pilot project for developing a Nationwide telephone network through which instantaneous reports on drug reactions occurring in hospitals could be made to F.D.A. The President was authorized to select an Ad Hoc Committee to discuss this matter with representatives of F.D.A.

6. President Johnson's Reorganization Program: Dr. Nicklas stated it had been suggested to him that the Society take an interest in Mr. Johnson's plan for reorganizing the District Government, particularly with reference to the portions of the plan dealing with health. The Board agreed that its Chairman, Dr. Corley, and President Ecker confer concerning the selection of a committee to consider this.

7. "Usual and customary fees": Dr. Camalier reported that the use of "usual and customary fees" by Blue Shield was gaining impetus throughout the country and would probably be adopted by Medical Service of D. C. in the near future. There was some question as to which should establish usual and customary fees, Medical Service or the Medical Society. Under the Medicare program the law speaks of "usual and customary fees" but the 3 conditions for determining such fees actually negate any possibility of Medical Service really paying usual and customary fees except in those situations where cases are referred to the Medical Society's Fee Review Committee.

There being no further business, the meeting was adjourned.



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## Meetings

**The International Doctors in Alcoholics Anonymous** will meet this year at Airlie in Warrenton, Va., beginning Friday, August 11, and ending at noon, Sunday, August 13. Membership is unnecessary; any interested physician is welcome. Advance reservations are required and should be addressed to Dr. Earl H. Mitchell, 3509 Dunlop Street, Chevy Chase, Md. 20015.

**"Drugs from the Sea,"** the first symposium of its type, will be held at the University of Rhode Island College of Pharmacy in Kingston, R. I., August 27, 28 and 29. It is sponsored by the Marine Technological Society, the Bio-Instrumentation Advisory Council of the American Institute of Biological Sciences, and the URI College of Pharmacy. Some 200 scientists are expected to attend.

## General News

In a letter of May 12, Dr. F. J. L. Blasingame, Executive Vice President of the American Medical Association, announced that the **second AMA-ERF fund solicitation mailing** for 1967 would soon go out. His letter stated that the amount of loans under the program has been limited to $750 instead of $1,500 per year due to lack of guarantee funds. The AMA-ERF now has in excess of $35,000,000 out on loan to approximately 19,000 students, interns and residents.

Two new publications have been released by the National Institutes of Health.

**" 'Red is the color of hurting': Planning for Children in the Hospital"** is based on proceedings of the workshop, Mental Health Planning for Pediatric Hospitals, held in New York in April 1965. A publication of the National Institute of Mental Health, it is available from the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C. 20402, at 55 cents per copy.

**"Eye Research,"** prepared by the National Institute of Neurological Diseases and Blindness, has been written for the general reader. A 44-page illustrated pamphlet, it reviews the known causes and current treatments for more than 20 blinding disorders as well as the latest research findings. "Eye Research," PHS Publication No. 1502, may be purchased from the U. S. Superintendent of Documents for 35 cents a copy.

Effective July 1, **Georgetown University School of Medicine** is adding 2 administrative staff members. They are **Dr. John F. Stapleton and Dr. Andre E. Hellegers.**

**Dr. Stapleton, Medical Director of Georgetown Hospital and Associate Dean of the School of Medicine**

Dr. Stapleton, who graduated in medicine from Georgetown in 1945, returns as Medical Director of the Hospital and Associate Dean of the School of Medicine. He will succeed Dr. Desmond O'Doherty, who has served as Acting Medical Director for the past 18 months.

After completing a residency in cardiology at Georgetown in 1951, Dr. Stapleton joined the faculty as Instructor in Medicine. In 1954 he went to Worcester, Mass., as Director of Medical Education at St. Vincent Hospital, an affiliate hospital of Georgetown. After 11 years in Worcester, he accepted a position at Woman's Medical College of Pennsylvania in Philadelphia as Associate Professor of Medicine and head of the Cardiovascular Division in the Department of Medicine.

Dr. Hellegers, newly appointed Professor of Obstetrics and Gynecology, comes to George-

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town from Johns Hopkins University where he was Associate Professor of Obstetrics and Gynecology. He is known internationally for his work in obstetrical and gynecologic physiology, and the psychology, ethics and law of birth control and abortion.

Born in The Netherlands, Dr. Hellegers received his medical education at Edinburgh University, Scotland. In 1953 he came to the United States and has been associated with Yale and Johns Hopkins Universities. He is consultant to the National Institute of Neurological Diseases and Blindness and to the National Institute of Child Health and Human Development. He is President-elect of the Society for Gynecologic Investigation.

**The Washington Academy of Surgery** elected the following officers at its meeting, May 8, at the Kennedy-Warren:

Dr. J. Blaine Harrell, *President*; Dr. Roy G. Klepser, *Vice President*; Dr. Ralph D. Whitley, *Secretary-Treasurer*; and Dr. Hamilton Dorman, *Assistant Secretary-Treasurer*.

Drs. Frederick B. Brandt, George A. Higgins and James H. Scully were elected to the Council for 2-year terms.

At this meeting the Annual Essay Awards for residents and interns in surgery were announced. Dr. Conrad Wesselhoef, Resident in Surgery at Children's Hospital, took first place for his paper on "Intramural Colo-anostomy for the Surgical Treatment of Hirschsprung's Disease." Dr. Jorge Betancourt, of the Washington Hospital Center, placed second, and Dr. William Tunnell, of Children's and Dr. Paul Herwick, of George Washington, received Honorable Mention. Dr. Wesselhoef read his paper during the scientific program.

**The George Washington University Medical Alumni Association** elected new officers in May. They are:

Dr. William Brainin, *President-elect*; Dr. James A. Dusbabek, *First Vice President*; Dr. Jack Kleh, *Second Vice President*; Dr. Charles E. Smith, *Secretary*; and Dr. Jerome W. Canter, *Treasurer*.

Dr. George Speck, of Alexandria, Va. retired as President and has been succeeded by Dr. Jerome H. Epstein, of Bethesda, Md.

**The Pan American Medical Society** has elected the following new officers for 1967:

Dr. Seymour Alpert, *President*; Dr. Charles J. Savarese, *Vice President*; Dr. Hector E. Castro, *Secretary*; and Dr. Chalon Rodriguez, *Treasurer*.

**Georgetown University School of Medicine** is one of 8 schools to receive a grant of $5,000 from the Dermatology Foundation of New York to assist in the training of skin disease specialists. Dr. Peter N. Horvath, Clinical Associate Professor of Dermatology, will direct the training program.

**Mr. Milton Golin,** who has served as Assistant to the President of the Pharmaceutical Manufacturers Association since 1960, has been **named Editor and Vice President of Physicians International Press, Inc.,** with offices in the Dupont Circle Building in Washington. In his new position Mr. Golin will assume editorial supervision of *Ob. Gyn. News* and *Pediatric News*. While at PMA he produced *Medicine at Work,* a monthly magazine he created in 1956 as a section of the *Journal of the American Medical Association.* He also was founding editor of *Medicolegal Digest.*

# Personals

**Dr. Howard E. Ticktin** received the 1967 Alumni Service Award from the General Alumni Association of the George Washington University at the 1967 Awards Dinner, June 2, held at the Mayflower Hotel. Dr. Ticktin is Associate Professor of Medicine at the University and heads its Clinical Division at D. C. General Hospital.

Twenty-five Year Awards presented for teaching service went to the following physicians: **Drs. Ruth B. Benedict, Frederic D. Chapman, and Lawrence J. Thomas,** Assistant Clinical Professors of Medicine; **Dr. Catherine Birch,** Assistant Clinical Professor of Otolaryngology; **Dr. Herbert H. Diamond,** Clinical Instructor in Pediatrics; **Drs. Julius R. Epstein and Morton S. Kaufman,** Assistant Clinical Professors of Obstetrics and Gynecology; **Dr. J. Blaine Harrell,** University Surgeon; **Dr. Jacob J. Weinstein,** Assistant Clinical Professor of Surgery; **and Dr Richard W. Wilkinson,** Associate Clinical Professor of Ophthalmology.

The seniors of the School of Medicine dedicated their student yearbook, the 1967 "Speculum," to **Dr. Harold Stevens,** and presented him with a special copy at their banquet at the Willard Hotel, June 1. In praise of Dr. Stevens, who became Professor and Chairman of the Department of Neurology in 1955, the Class wrote: "We respect both his achievements as a scholar and his dedication to his students. As a teacher he imparts his knowledge with enthusiasm and skill. As a man he offers us a fine example of the physician which one day we hope to be."

**Dr. William P. Herbst** was elected President of the American Association of Genitourinary Surgeons at its Annual Meeting in Westchester, New York, on May 18.

**Dr. Paul R. Wilner** received the 1967 Annual Award of Honor from the Georgetown Clinical Society at its "Old Timers" dinner, March 15, at the Kennedy-Warren, for his outstanding contributions to medicine and to Georgetown University.

**Dr. Robert J. Coffey** has been appointed by the D. C. Commissioners to serve on the Public Health Advisory Council for a term of 3 years, expiring February 13, 1970.

**Dr. John F. Maher,** Assistant Professor of Medicine at Georgetown University, was designated Editor of *Clinical Research,* the official publication of the American Federation for Clinical Research, at the Annual Meeting of the Federation in Atlantic City, April 30.

**Dr. William B. Walsh,** founder and President of Project HOPE, received the Council Award, the highest honor of the State Medical Society of Wisconsin, at a banquet, May 10, during the Society's Annual Meeting in Milwaukee. Dr. Walsh accepted the award from Dr. James C. Fox, of La Crosse, President of the Council.

The District of Columbia Red Cross Chapter honored some 950 volunteers and staff members who had given 5 or more years of service to the Red Cross, through the D. C. Chapter, at a Recognition Ceremony, May 9, in the Departmental Auditorium. **Dr. Roy Lyman Sexton** was cited for serving 44 years in Safety Services. **Dr. W. Montague Cobb,** who has served in the same division for more than 10 years, **and Dr. Herbert P. Ramsey,** over 5 years, also received Certificates of Appreciation.

**Dr. Alan M. Weintraub** was elected to fellowship in the American College of Physicians on April 9.

# Obituaries

## William Arthur Morgan, M.D.

(1890–1967)

Dr. William A. Morgan, who had practiced otolaryngology in Washington for 45 years, died, May 16, 1967, at Doctors Hospital, where he was Chief Emeritus of Otolaryngology. His offices were at 1835 Eye Street, N.W.

Dr. Morgan was born in Wake County, N. C., December 6, 1890. He attended the University of North Carolina and graduated in medicine from the Medical College of Virginia in 1917. He interned at St. Vincent's Hospital, New York, in general surgery and trained in his specialty at Episcopal (Washington) and Manhattan (New York) Eye, Ear and Throat Hospitals.

During World I he served as a Lieutenant in the Naval Medical Corps. Later he became a Major in the Army Medical Corps Reserve and served as a medical advisor to the Army Air Corps in World War II.

He was chosen for 2 medical missions by the Department of the Interior, the first to the Pribilof Islands in the Bering Sea off Alaska in 1944 and the second to the Virgin Islands and Puerto Rico in 1948.

In 1945, deeply concerned over the health problems in the Dominican Republic, where he had visited on vacations, he offered to operate without charge on any children who needed nose and throat operations. It was reported that he performed over 1,500 operations during 2 visits that year. The following year the Dr. William A. Morgan Hospital in Trujillo City was named for him in appreciation of his volunteer work, which included the training of local doctors in his specialty. Until 1961 he had continued to visit the Dominican Republic for a month out of every year to treat patients and to help in the development of health programs.

Dr. Morgan was otolaryngologist at Garfield and Sibley Memorial Hospitals before joining Doctors as head of the Department of Ear, Nose and Throat when the Hospital was opened in 1940.

A diplomate of the American Board of Otolaryngology, he was a member of the American Medical Association and an Active member of the Medical Society of the District of Columbia from 1925 until 1960. He belonged to the Chevy Chase and Burning Tree Country Clubs.

He leaves his wife, Mrs. Elizabeth Shumate Morgan, of their home, 2610 31st Street, N.W.; a sister, Miss Blanche Morgan, of New York City; and a brother, Mr. Harvey Morgan, of North Carolina.

## George Byron Roth, A.B., M.D.

(1879–1967)

Dr. George B. Roth, Emeritus Professor of Pharmacology of George Washington University School of Medicine, died, May 23, 1967, at Doctors Hospital after a short illness.

Born in Mt. Eaton, Ohio, May 22, 1879, he was a graduate of Michigan Military Academy, Orchard Lake, Mich. He received both his A.B. and M.D. degrees (the latter in 1909) from the University of Michigan, where he remained until 1913 to teach pharmacology.

Dr. Roth was a laboratory pharmacologist with the U. S. Public Health Service from 1913 to 1921. He served on the staff of Western Reserve University as Assistant Professor of Pharmacology, 1921–1924, and came to George Washington University as Professor and Chairman of the Department of Pharmacology in 1924. He retired with the rank of Emeritus Professor in 1945.

He served from 1952 to 1964 as a member of the D. C. Basic Science Board for Medical Licensure.

A Fellow of the International College of Anesthetists, Dr. Roth was a member of many professional and scientific societies, including the American Medical Association, American Society of Pharmacology and Experimental Therapeutics, Society for Experimental Biology and Medicine, and the American Physiological Society. He had been an Associate member of the Medical Society of the District of Columbia since 1926. He was a Mason and a member of the Audubon Society and the Cosmos Club.

His book, "Practical Pharmacology," was published in 1929. He contributed numerous articles to the literature on pharmacology and other scientific subjects.

An avid rose grower, he was a member of the Potomac Rose Society and the recipient of many of its awards.

He leaves his wife, Mrs. Dorothea Payne Roth, of the home address, 3814 T Street, N.W., and a daughter, Mrs. Dorothy Roth Wilson, of Kansas City, Mo.

# New view of an oral contraceptive at work

Although suppression of ovulation remains the primary mode of action of oral contraceptives, newer knowledge indicates that products like Norinyl-1 — a combination of both low-dosage progestogen and estrogen for the full treatment cycle — may provide multiple action that helps explain their unexcelled record of contraceptive effectiveness. This report explores the possible secondary protective mechanisms offered by combined hormonal administration.

Accumulating evidence has indicated that sparse, highly viscous cervical mucus has a possible adverse effect on the motility and survival of spermatozoa.

The estrogen-opposing progestational ingredient of Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.) changes the usual midcycle picture of a thin, watery cervical mucus. The result — a built-in barrier that appears to inhibit sperm from reaching the ovum should one be released. The inset in the adjoining photograph shows immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

See last page for contraindications, precautions, side effects and dosage.

# How the estrogen-opposing action of Norinyl-1 creates cervical mucus that may be hostile to sperm penetration

Normally, estrogen activity during the fertile midcycle stimulates the production of a profuse and watery cervical mucus that permits maximum sperm motility and promotes penetration.

But what happens when Norinyl-1 is administered? Its potent progestogen, norethindrone, opposes estrogen stimulation of cervical mucus. Consequently, the amount of mucus decreases and its viscosity increases. This results in a sparse but thick mucus barrier that appears to diminish the vitality of the sperm and to impair its powers of penetration.

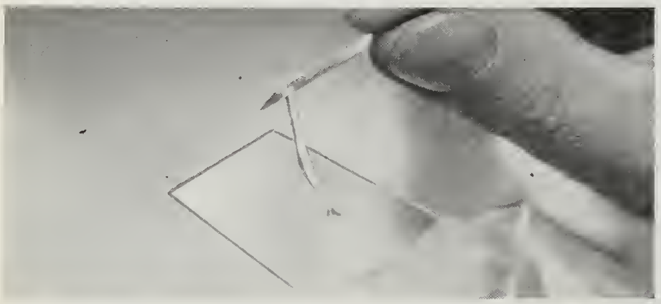
## The role of viscous cervical mucus as a secondary action of Norinyl-1

In a report on 89 patients taking this medication,* cervical mucus obtained from cycle day 5 to cycle day 29 appeared scant and thick and exhibited little or no Spinnbarkeit.

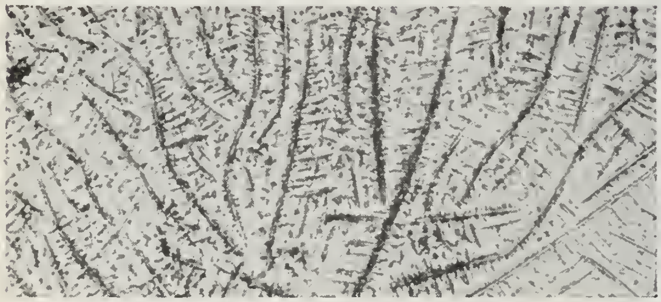
In the opinion of this investigator, the effect on cervical mucus may be sufficient to prevent conception.

*Cohen, M. R.: Symposium: Mechanisms of Action of Low Dosage Oral Contraceptive, Yale University Medical Center, New Haven, Conn., April 6, 1967.

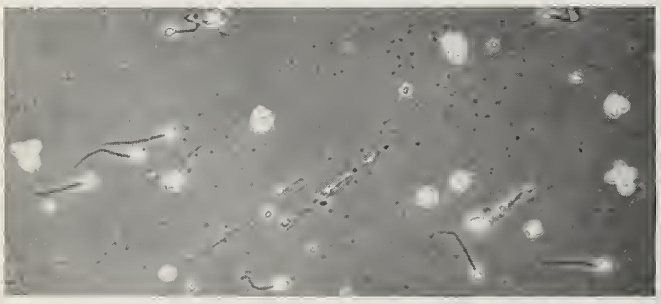
### Normal cervical mucus at midcycle in untreated patient is known to permit sperm motility... promote sperm penetration.



Cervical mucus is thin and watery with a stretchability (Spinnbarkeit) of 15 to 20 cm.

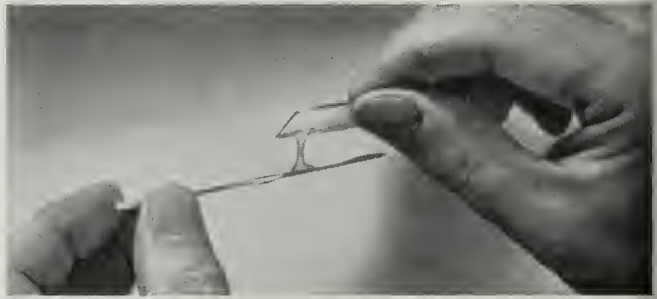


Thin, watery mucus crystallizes into this well-defined, fernlike pattern within a minute.

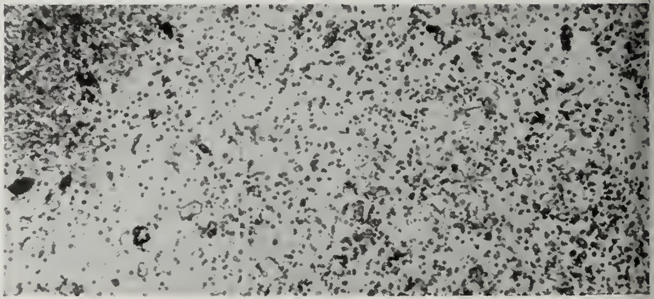


Spermatozoa appear healthy, are active and freemoving.

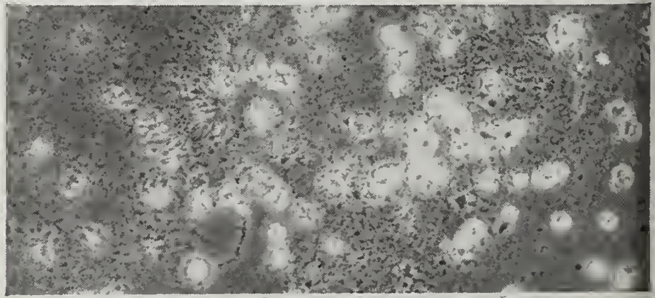
### Viscous cervical mucus at midcycle produced by Norinyl-1 appears to impair sperm vitality... inhibit penetration.



Cervical mucus is scanty, thick and viscous. Spinnbarkeit is 1 cm. or less.



In thick, viscous cervical mucus the fern pattern is poorly defined or absent.

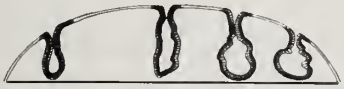


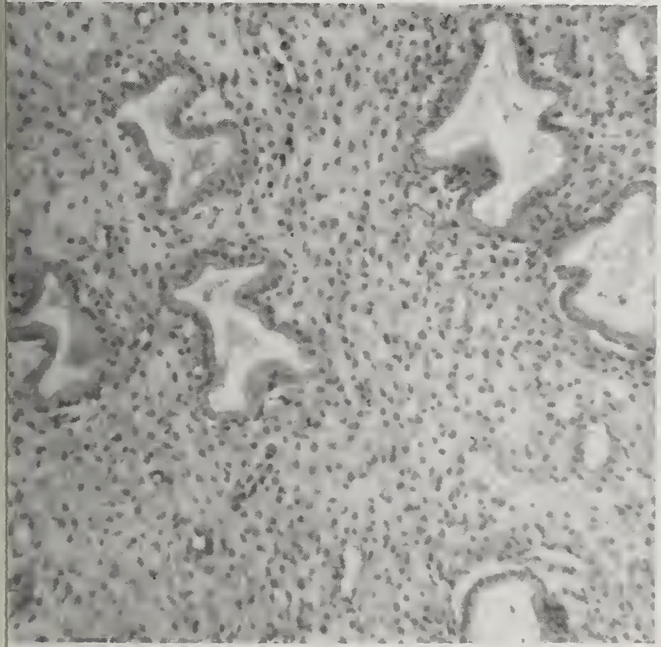
Immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

# How Norinyl-1 alters normal endometrial responses–another possible protective mechanism

et us suppose that an ovum is released—as occurs in an ccasional, rare case—and somehow a sperm succeeds in enetrating the cervical mucus barrier. Should this come about, ne additional action of Norinyl-1 may protect the patient rom unwanted pregnancy. The theory is that progestogen intake nakes endometrial tissue unreceptive to implantation.

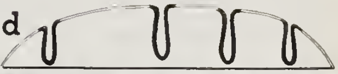
ndometrium of
ntreated patient

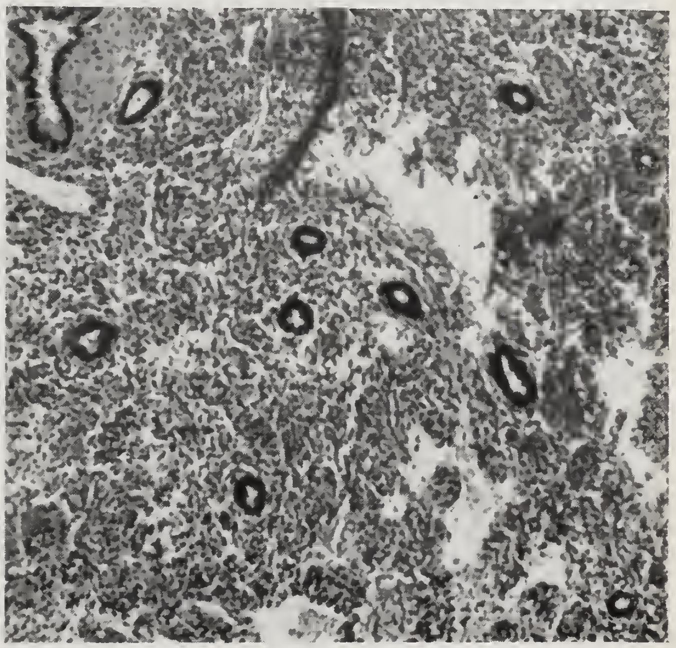




ormally, the endometrium progresses through proliferative phase stimulated by estrogen and a ecretory phase stimulated by progesterone. uring the secretory phase the endometrium is eceptive to the fertilized ovum.

Endometrium produced
by Norinyl-1





When Norinyl-1 is administered its progestogen component—norethindrone—accelerates the secretory phase and suppresses glandular and vascular development.

new
Norinyl®-1
tablets
(norethindrone 1mg. c̄ mestranol 0.05mg.)

ee last page for contraindications, precautions, side effects and dosage.

effective fertility control on half the previous dosage

maintains ratio of the established norethindrone/mestranol combination

lower cost

# new Norinyl-1® tablets

(norethindrone 1mg. c̄ mestranol 0.05mg.)

Reduction of oral contraceptive dosage to lowest effective levels has become a well-accepted principle of conservative medical practice In keeping with this view, Norinyl is now available in a new strength in which *both* norethindrone and mestranol are reduced 50 percent Studies show that Norinyl-1 achieves fertility control with only 1.05 mg. of combined progestogen and estrogen per tablet.

Norethindrone was first reported for use as a progestational agent in human beings in 1955. Norethindrone 2 mg. with mestranol 0.1 mg., as an oral contraceptive, is currently in use by over 2,000,000 women Clinical experience now establishes that Norinyl-1 also amply meets the criteria of reliability and safety.*

*Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965.

PRESCRIBING INFORMATION

**Contraindications:** 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

**Warnings:** 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of Norinyl-1 in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

**Precautions:** 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with Norinyl-1. Therefore, if such tests are abnormal in a patient taking Norinyl-1, it is recommended that they be repeated after the drug has been withdrawn for 2 months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibroids may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac, or renal dysfunction, require careful observation. 5. Although a cause and effect relationship has not been established, Norinyl-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, as in all cases of irregular bleeding *per vaginam*, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged Norinyl-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Norinyl-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. A cause and effect relationship has not been demonstrated. 11. Because of the effects of estrogens on epiphyseal closure, Norinyl-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask the onset of the climacteric. 13. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

**Side Effects:** The following adverse reactions have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma, breast changes (tenderness, enlargement and secretion), loss of scalp hair, change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, erythema multiforme, erythema nodosum, hemorrhagic eruption, migraine, rash (allergic), itching, rise in blood pressure in susceptible individuals, mental depression.

The following occurrences have been observed in users of oral contraceptives. A cause and effect relationship has not been established: thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory results may be altered by the use of oral contraceptives: increased bromsulphalein retention and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in $T^3$ values), metapyrone test, pregnanediol determination.

Other side effects reported to have occurred in association with use of this drug are dizziness, hirsutism, pains in legs, back, chest and abdomen, dysuria, drowsiness, vaginal discharge, libido increased and decreased, eruptions, hypermenorrhea, hypomenorrhea increased appetite, G.U. infections, varicose veins, abdominal fullness, acne, headache nervousness, allergies, blurred vision, pain in eyes, and itching in eyes. *For complete clinical data, see package insert.*

**Dosage and Administration:** 1. One tablet of Norinyl-1 is administered orally for 20 days beginning on day 5 of the menstrual cycle. (Count day 1 of the cycle as the first day of menstrual bleeding.) Repeat this dosage schedule for each cycle. 2. If no menstrual period occurs after a cycle of treatment (20 tablets) in which patient adhered to the schedule, the patient must be instructed to resume taking the Norinyl-1 tablets 7 days after the previous 20-day course was completed. For example, if the last pill of a previous cycle had been taken on a Sunday, then a new cycle of treatment should begin on the following Sunday. 3. In the postpartum woman, it is recommended that the first cycle of treatment should begin on day 5 of the first menstrual cycle. However, Norinyl-1 should not be administered during lactation.

**Availability:** Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.)—Dispensers of 20 and 60 and bottles of 250 tablets.

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BRIEF SUMMARY/**Indications:** Ambar suppresses appetite and helps offset emotional reactions to dieting. **Contraindications:** Hypersensitivity to barbiturates or sympathomimetics; patients with advanced renal or hepatic disease. **Precautions:** Administer with caution in the presence of cardiovascular disease or hypertension. **Side Effects:** Nervousness or excitement occasionally noted, but usually infrequent at recommended dosages. Slight drowsiness has been reported rarely. See package insert for further details.

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# BOOK REVIEWS

**Medical Department, United States Army: Radiology in World War II.** Colonel Arnold Lorenz Ahnfeldt, MC, USA, Editor in Chief; Kenneth D. A. Allen, M.D., Editor for Radiology; Elizabeth M. McFetridge, M.A., Associate Editor; and Mindell W. Stein, B.Sc., Associate Editor. Prepared and published under the direction of Lieutenant General Leonard D. Heaton, The Surgeon General, United States Army. Price, $8.25. Pp. 1087, illustrated. Washington, D. C. 20402: U. S. Government Printing Office, 1966.

The official history of the Medical Department of the U. S. Army in World War II has been prepared by the Historical Unit, U. S. Army Medical Service, and published under the direction of The Surgeon General, U. S. Army, in 2 series, the administrative or operational series and the professional, or clinical and technical, series, and this present book is one of the volumes published in the latter series.

This book is a rather comprehensive and detailed record of military radiology in World War II. A brief historical review of military roentgenology before and during World War I is also included.

This volume records the multiplicity of problems faced by the military in radiologic personnel and training, equipment and supply, and the methods by which these tasks were accomplished.

The Mediterranean, European, and Asiatic-Pacific Theatres of Operation have been discussed and reviewed separately at length. The role of radiology in the development of the atomic bomb has been faithfully recorded.

This book will be of interest primarily to the countless and nameless men who participated in this phase of American history. It will be of interest from a technical standpoint in serving as a permanent record of how actual progress can be accomplished in moments of uncertainty and stress. From a medical standpoint many of the unusual diseases and particularly those dealing with trauma are recorded.

Charles E. Bickham, Jr., M.D.

**Resuscitation of the Newborn Infant and Related Emergency Procedures. Principles and Practice,** 2nd ed. Edited by Harold Abramson, A.M., M.D. Price, $16.50. Pp. 411, illustrated. St. Louis: Mosby, 1966.

The second edition of "Resuscitation of the Newborn Infant," edited by Dr. Abramson, is an attempt to bring together the latest developments in neonatology since 1960, when the first edition was published.

This edition contains 411 pages and includes 4 new chapters. These are: "The Acute Anemias of the Perinatal Period," "Surgical Emergencies in Respiratory Difficulties of Newborn Infants," "Infections of the Newborn," and "Fluid and Electrolyte Therapy in the Newborn Infant."

The book is designed to incorporate recent knowledge on the causes, the pathogenesis, early detection, and treatment of diseases that produce respiratory difficulties in the very young. Such a subject can only be dealt with adequately by a team of doctors vitally interested and knowledgeable on the resuscitation of the newborn. This book is indeed written by such a group. All the contributors are active members or consultant members of the Special Committee on Infant Mortality of the Medical Society of the County of New York.

However, it tends to be sketchy in many subjects. The attempt to cover so much in less than 500 pages has caused rather synoptic discussions. This can be overcome by the fact that the references are up to date and the interested reader can read the original articles for details. Since the book was edited in June 1966, the most recent references are in 1965.

The present edition has some very good tables, and the chapter on "Surgical Emergencies in Respiratory Difficulties of the Newborn Infants" has some of the most interesting and unusual X-rays to be found.

The book emphasizes that the initial evaluation and resuscitation should be carried out by a person experienced in the problems peculiar to early intrauterine existence. I like the description of the Recovery Nursery for newborn infants where the "newborn infants are at last regarded as individuals." One couldn't agree more that "the efficient operation of the recovery nursery will be conditioned by the degree of coöperation between the obstetric and pediatric services and all essential ancillary medical services in meeting the basic problem, that is, the reduction of preventable neonatal morbidity and death."

This edition should be read by anyone who is dealing with newborns, such as nurses, medical students, and residents in obstetrics, pediatrics and anesthesia. It is not a book for those deeply involved in research in the field of neonatology.

Artemis P. Simopoulos, M.D.

**Vascular Complications of Diabetes Mellitus, with Special Emphasis on Microangiopathy of the Eye.** Edited by Samuel J. Kimura, M.D., and Wayne M. Caygill, M.D. Price, $19.75. Pp. 277, with 124 illustrations. St. Louis: Mosby, 1967.

This excellent and stimulating symposium from the University of California at San Francisco combines concise and cohesive editing with a thorough review of the present concepts of diabetes as it affects the microcirculation of the eye.

The relationship between the capillary mesangial cells in diabetic glomerulosclerosis, the pericytes of the peripheral capillaries, and the mural cells of the retina are discussed in depth with appropriate electron microscopic sections. Their significance in relation to the thickening of the basement membranes of the capillaries seen in diabetes and the similarity of such changes to other vascular inflammatory conditions are demon-

*(Continued on page 36)*

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## Book Reviews

(*Continued from page 35*)

strated in India ink and trypsin-digestion preparations.

Covering fluorescein angiography, the current concepts of insulin, insulinogenic reserve, immunologic reactions to insulin, and insulin antagonists are discussed. Biochemical changes in plasma lipids and lipoproteins and the physiologic implications of alterations in aqueous secretion are presented.

Concluding the symposium is a lucid presentation of the various anterior pituitary approaches to therapy, and the current status of their application is frankly discussed. There is only brief mention of the status of photocoagulation in clinical retinopathy.

The striking lack of knowledge of the natural course of the disease is the most glaring deficiency, not of the symposium but of diabetic research in general. The 50 per cent incidence of spontaneous remission in one series compares favorably with the 50 per cent incidence of improvement in one series of pituitary ablation. It is well to remember the patients with accelerated hemorrhagic retinopathy are at an end stage of an accelerated vascular deterioration involving the entire circulatory system with a limited life expectancy.

A. Raymond Pilkerton, M.D.

**Congestive Heart Failure.** Ralph M. Myerson, B.S., M.D., F.A.C.P., and Bernard H. Pastor (deceased), A.B., M.D., F.A.C.P. Price, $12.85. Pp. 174, illustrated. St. Louis: Mosby, 1967.

This is a book noncontroversial in content and straightforward in presentation. It is a compilation of observations on the causes (chapter 2), diagnosis (chapter 3), and treatment (chapters 4, 5 and 6) of congestive heart failure.

The authors accomplished what they intended, which was "... to correlate the fundamental disturbances present in congestive heart failure with the clinical picture and therapy." This has resulted in a small book beginning with a brief discussion on muscle dynamics, histochemistry, and circulatory physiology, and relating this basic information to the syndrome of congestive heart failure.

Noteworthy is the fact that 13 pages are devoted to the etiology and pathogenesis of congestive heart failure, while 77 are required to discuss its treatment. This indicates that while we are unsure of the mechanisms involved in this symptom complex we are even more confused in regard to its treatment. The book, unfortunately, has done little to clarify either. In its defense, it has listed the possibilities.

The book's main difficulty rests more with its address to a number of disease processes based on a common symptom than to its lack of a scholarly approach to the subject. It is not a reference source. Footnotes are not used, and the selected reference lists are not extensive.

(*Continued on page 37*)

## Book Reviews

*(Continued from page 36)*

The book might find its greatest use as a small soft-back for senior medical students and medical house officers. It is also recommended for the practicing physician who in a short period of time needs to review this common clinical problem.

James R. Snyder, M.D.

**Ciba Foundation Study Group No. 23. Egg Implantation.** Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Maeve O'Connor, B.A. Price, $3.50. Pp. 112, with 25 illustrations. Boston: Little, 1966.

This little volume contains 5 basic science papers which were presented at a 1-day meeting in honor of Professor R. Courrier. Professor Courrier, now 70, is one of the world's leading scientists in the physiology and endocrinology of reproduction.

This meeting attracted the work and the discussion of an international array of scientists who were vitally involved in the subject. The titles of several of the papers are: "Recent Researches on Egg Implantation," "Placentation in the Rabbit Studied by Means of Sulfur$_{35}$," and "Some Mechanical Aspects of Trophoblast Penetration of the Uterine Epithelium in the Rabbit."

The reader quickly arrives at the conclusion which Sir Solly Zuckerman, the moderator, imparted: "The field is wide open and 2 years from now it may be just as wide open." Between the differences in species of the animals studied and the various interpretations by the scientists even with the same species, many facts have been observed but their significance is imprecisely understood.

One observation might serve as a theory for the mechanism of action of the intrauterine device. Dr. Psychoyos found that the traumatized endometrium of rats had an increased progesterone uptake. As a result, the endometrium matured prematurely, and the period of endometrial receptivity for the fertilized ovum expired prior to the ovum's arrival at the endometrium. Therefore, implantation was impossible. The IUD may act by traumatizing the endometrium, but this hormone reaction is species specific and has not been demonstrated in the human.

"Egg Implantation" presents some of the latest research and current thinking of many of the leading authorities in this field. The book would be of primary value to the clinician or basic scientist interested in the minute details of egg implantation.

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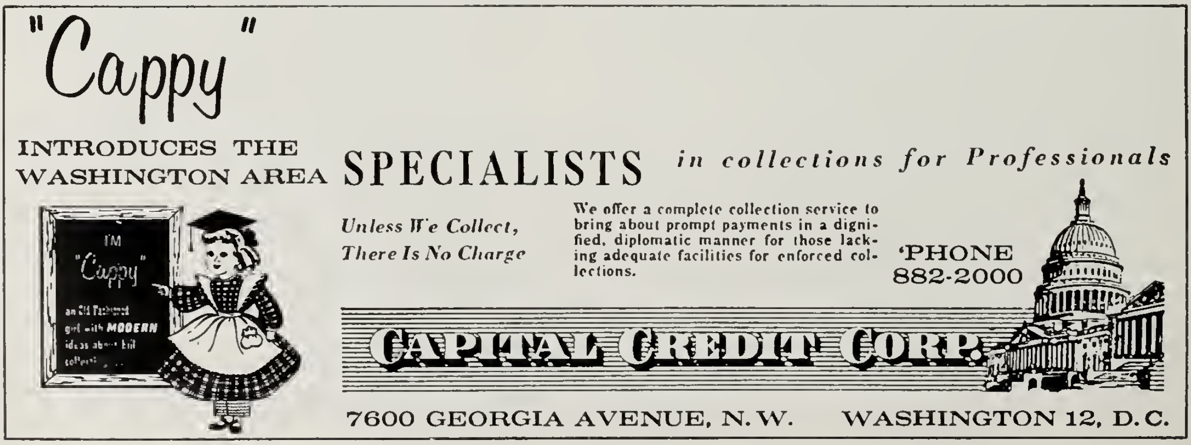

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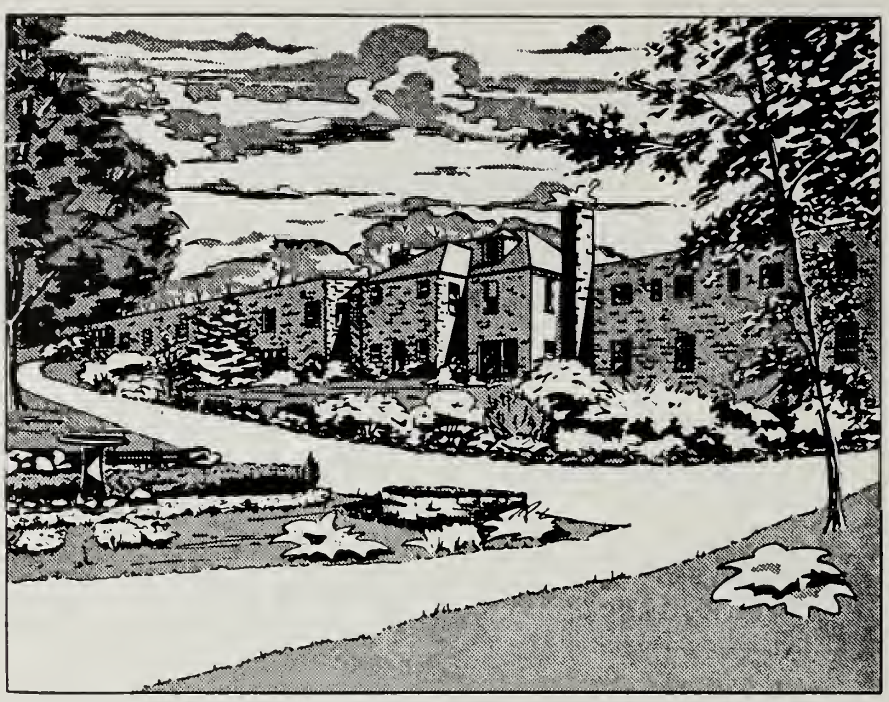

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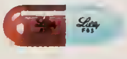

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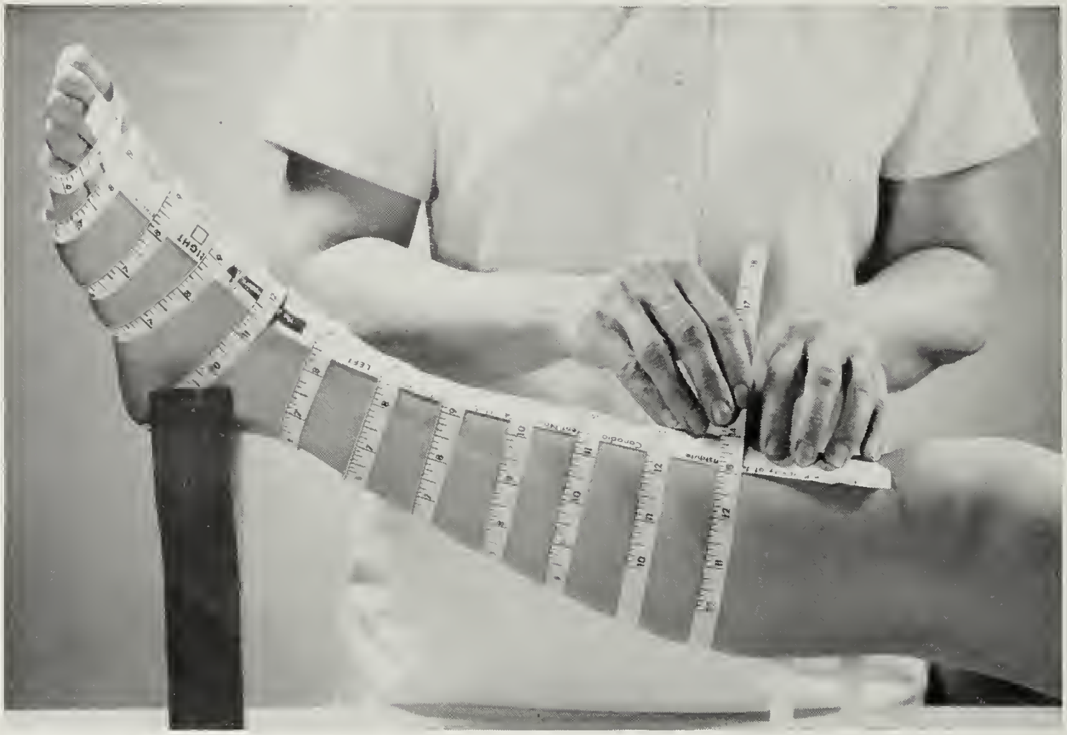

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**Precautions**: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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COLUMBIA HOSPITAL FOR WOMEN NUMBER

*August 1967* Vol. XXXVI · No. 8

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W. J. Jaffurs, M.D.

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**Placental Polyp Causing Puerperal Hemorrhage**
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**Repair of Vault Vesicovaginal Fistula**
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**Diagnosis of Subclinical Diabetes in Pregnancy**
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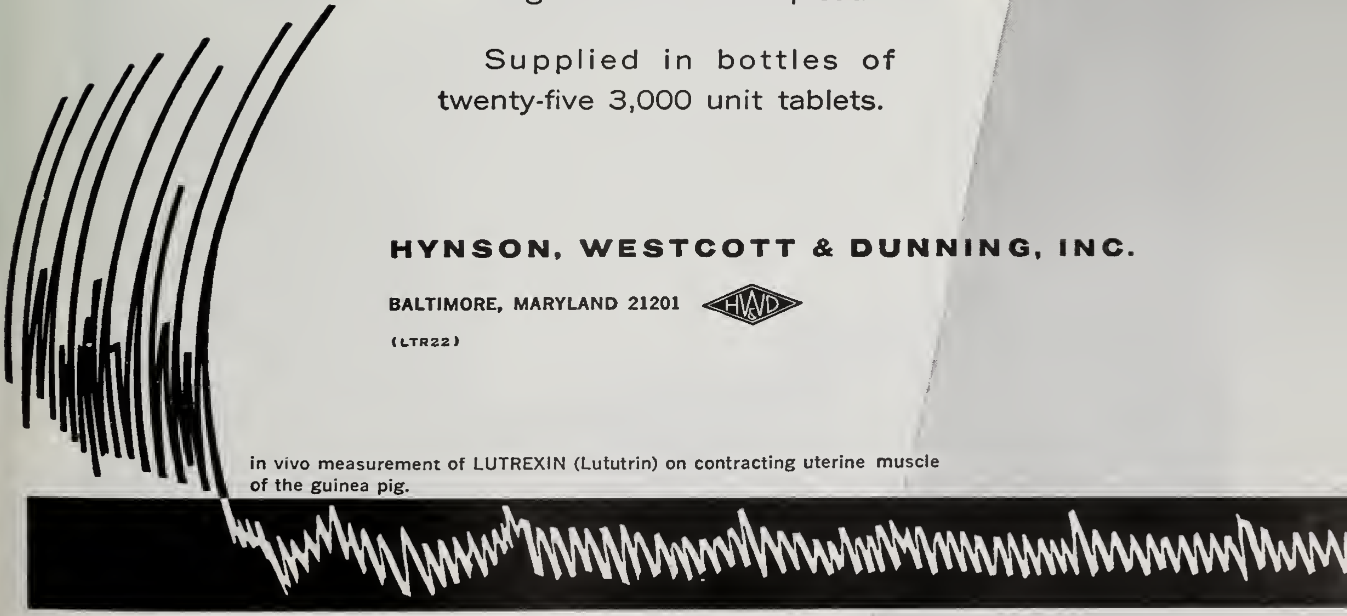

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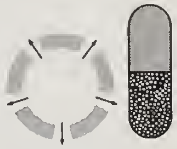

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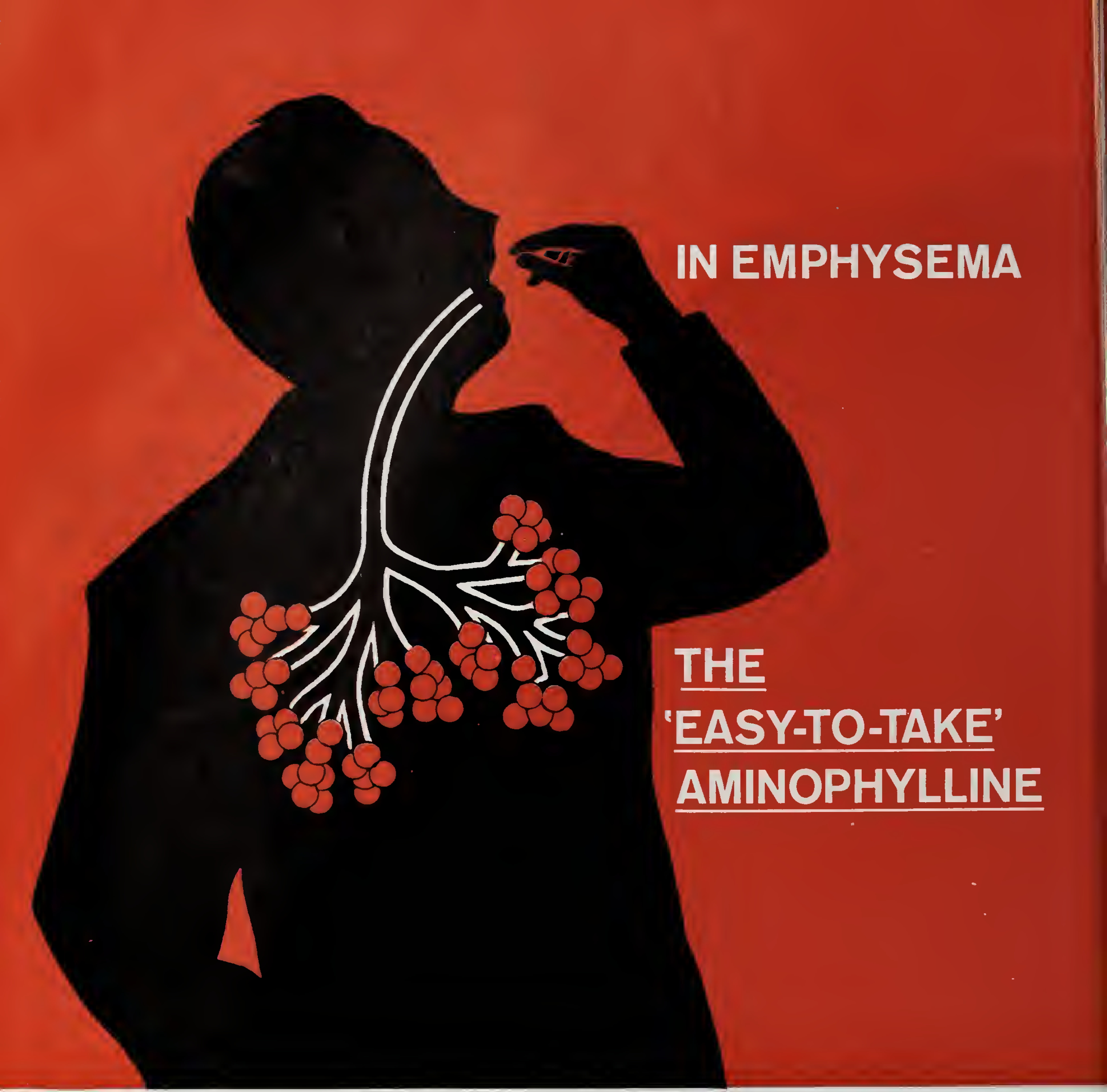

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# BOOK REVIEWS

**Clinical Management of Behavior Disorders in Children,** 3rd ed. HARRY BAKWIN, M.D., AND RUTH MORRIS BAKWIN, M.D. Price, $14.50. Pp. 652, illustrated. Philadelphia: Saunders, 1966.

There are few comprehensive books dealing with the understanding and management of psychopathology in children for the nonpsychiatrist and physician. The authors, a husband-and-wife pediatrician team, use the term "behavior disorders," thereby indicating something minor that any understanding pediatrician or counselor can handle. The fact is that they do cover the whole range of child psychopathology from learning disorders to childhood schizophrenia. Clear-cut organic diseases are omitted.

The authors' goal is very clearly to help fellow pediatricians feel competent, useful, and at home in the broad area of emotional illness. They can learn much about the impact of developmental disorders and parental attitudes on their patients. If the pediatrician has preferred to ignore emotional problems as unimportant, to deny them altogether, or to see some as organic illness, this book may help close the "credibility gap."

It is unfortunate that the Bakwins have found it so necessary to protect the pediatricians and their patients from child psychiatrists, child guidance clinics, family agencies, etc. before they decide that "emotionally ill children and their parents need the support and advice of the physician even though no specific treatment is available." Lest one be tempted to suggest treatment, the next sentence reads: "However, the practice of seeing at frequent intervals children for whom the probability of a beneficial therapeutic result is remote should be discouraged." I do not disagree with the sentence as it stands, but the implied assumptions are that the pediatrician should determine the indications for treatment and that the psychiatrist is likely to make impractical and hurtful treatment plans. "To advise psychiatric treatment when parents are unable to pay for it makes them feel inadequate and helpless; it compounds their misery and it often leads to interparental conflict." These sentences were added to the third edition; it is evident that the collaboration gap is not closing. Nowhere are the warnings balanced with indications for appropriate referral for evaluation and possible treatment.

The thoughtful and concerned pediatrician may feel very lonely with the responsibilities thrust upon him. He will avoid overconcern for minor behavior problems, but he will be bewildered by the massive job of managing the home and school environment, listening to the child and guiding the parents when he has to treat severe phobias, compulsions, character disorders, etc. He is not even given a consistent theoretical frame of reference for the understanding of personality growth and development.

There do not seem to be significant changes from the 1960 edition. The book is a little bit shorter, the cover brighter, the pages glossier. An additional 50 pages of more recent material on developmental disabilities, battered child and other syndromes have been added. The organization and format are the same.

EDWIN S. KESSLER, M.D.

**Proceedings of the Workshop on Ureteral Reflux in Children.** JAMES F. GLENN, M.D., Scientific Editor. Price, $2.50. Pp. 219. Washington, D. C.: National Academy of Sciences-National Research Council, 1967.

This workshop, which was held November 11–12, 1966, was sponsored by the Committee on the Genito-Urinary System, Division of Medical Science, National Academy of Sciences-National Research Council. Participants in the workshop were recognized authorities in basic science and clinical urology. This book contains the best bibliography in the field that is now available.

WILLIAM P. HERBST, M.D.

**Atlas of Vascular Surgery,** 2nd ed. FALLS B. HERSHEY, M.D., F.A.C.S., AND CARL H. CALMAN, M.D., F.A.C.S. Price, $19.50. Pp. 318. Illustrated by Kathryn Murphy Masterson and William R. Schwarz. St. Louis: Mosby, 1967.

This book represents the most recent and probably to date the best attempt to graphically illustrate the common procedures used in vascular surgery today. As with any atlas of surgical technique, there are points that individual surgeons would disagree upon in the management and treatment of specific problems. However, as a general guide to surgical residents and surgeons already in practice who have occasion to perform vascular surgery, this book should prove to be as useful as its standard companion in general surgery, Zollinger's Atlas of Surgery. The volume has the same shortcomings as any atlas. It is not nor is it intended to be a textbook of vascular disease. Of necessity, the chapters dealing with principles of vascular disease, arteriography, and preoperative and postoperative evaluation and management must be brief.

The illustrations are clear and well-labeled. In general, most of the techniques described are becoming standard operative techniques for vascular surgery and will probably remain so for the immediate future. Many recent introductions in vascular surgery, such as the use of the Fogarty embolectomy catheter or electrofulgeration in the treatment of varicose veins, are covered.

The book should be a welcomed addition to surgical residents. A word of caution, however, to the inexperienced regarding all surgical atlases. Step-by-step procedures in surgery are certainly nice as long as the operation progresses as described in the atlas or the patient's condition continues as described in the atlas. It is when the unexpected is found at the time of surgery or complications develop that you find the atlas to be deficient and surgical experience to be the physician's best friend.

JOSEPH F. SCHANNO, M.D.

*(Continued on page 12)*

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## Book Reviews

*(Continued from page 11)*

**The Human Heart. The Layman's Guide to Heart Disease.** Brendan Phibbs, M.D., F.A.C.P., with contributions from Lane Craddock, M.D., George Griffith, M.D., Robert T. Patrick, M.D., and Colin H. M. Walker, M.D. Price (paper), $4.95. Pp. 253, with 72 illustrations. St. Louis: Mosby, 1967.

Dr. Phibbs and his 4 collaborators wrote this book to educate the layman and to answer his questions. It gives the basic facts about how the heart is made, how it works, what can go wrong with it, and what can be done to cure or help it. It does this very clearly and concisely with adequate diagrams. It gives a short course in cardiac first-aid for the patient's own benefit and for anyone he might unexpectedly have "to attend" until medical help arrives. It explains simply the laboratory methods of cardiac evaluation and details the advances that cardiac surgery has made to the present.

The book in its entirety is a good "textbook" of cardiology for the layman. There may not be any patient who would be interested personally in every chapter; however, it can be confidently recommended for the patient frequently seen who has coronary artery disease, hypertension, valvular heart disease, or pulmonary heart disease, or for the anxious parents of those with congenital heart malformations. As the authors state, heart patients should know as much as possible about the particular heart disease they have as this knowledge may mean better coöperation and may mean the difference between success or failure of many kinds of treatment.

Richard B. Perry, M.D.

**Clinical Pathology. Interpretation and Application,** 4th ed. Benjamin B. Wells, M.D., Ph.D., and James A. Halsted, M.D. Price, $11.50. Pp. 708, illustrated. Philadelphia: Saunders, 1967.

This book is divided into system disease descriptions accompanied by laboratory test applications. The authors preface most disease descriptions with a summary of pathophysiology. The last section is a compendium of common office laboratory procedures. The design is well executed and the text readable. The format is not tailored to the physician in search of a clinical explanation for an abnormal test.

The authors define their audience as "physicians, medical students, technologists, nurses, and other members of the health service professions who wish to learn how the clinical laboratories serve the practice of medicine." The book is geared to the less trained of this vast audience. The body of the text is an evaluation of diseases by tests of long-standing usage. The only exception to this statement is a chapter on clinical genetics which is a current summary of the field. While the authors state they are not about to discuss every laboratory assay, a 1967 text of clinical pathology without

*(Continued on page 13)*

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mention of LDH isozymes, chemical profile interpretation and composition, $T_4$, steroid assays other than 17-KGS or 17-OHCS, immuno-electrophoresis, fluorescent treponemal antibody procedure, and thromboplastin regeneration coagulation test is not reasonable. Compensation for this fault is possible by the inclusion of a strong basic approach to test value in disease. Unfortunately, the introductory chapter is skimpy and the reader is not given a thorough foundation to personally evaluate a test based on statistics, quality control, specimen stability, inherent percent test accuracy, or instrumentation. The lack of emphasis in the newer dimensions of this exploding field of clinical pathology in medical practice gives the book an archaic air.

Many may fill a gap in their library with this volume; however, a basic, current, comprehensive text describing the medical practice of clinical pathology remains unpublished.

Joseph T. Sobota, M.D.

**Ciba Foundation Symposium. The Thymus: Experimental and Clinical Studies.** Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Ruth Porter, M.R.C.P. Price, $15.00. Pp. 538, with 96 illustrations. Boston: Little, 1966.

This book is the record of an international symposium on the thymus held recently in Melbourne, Australia, and sponsored by the Ciba Foundation.

The structure and function of the thymus in the experimental animal and in man are examined in great detail. The role of the gland in the development and function of the lymphocyte and mast cell is studied at length, also its role in immunology, leukemogenesis, carcinogenesis and auto-immune disease.

Most of the papers are followed by panel discussions, which are excellent and frequently more informative for the inexpert than the highly technical papers preceding them.

There are few firm conclusions, but it is suggested that:

1. Multipotential cells from the bone marrow are differentiated into immunocytes in the thymus.
2. Only 5 per cent of these cells have immune patterns acceptable to the body, and these cells migrate to lymph nodes. The rest are destroyed in the thymus.
3. Plasma cells are derived from lymphocytes.
4. Several hormones are produced by the thymus. They regulate lymphocyte maturation, migration, and transformation into plasma cells.

The studies of auto-immune mechanisms suggest that myasthenia gravis may fall into this category. There is support for the standard view that thymectomy is of most value in young women with myasthenia gravis who do not have thymoma.

The book is an excellent reference work for students of the form and function of the thymus, and the final chapters on auto-immune disease contain much that is of interest to the clinician.

Nicholas P. D. Smyth, M.D.

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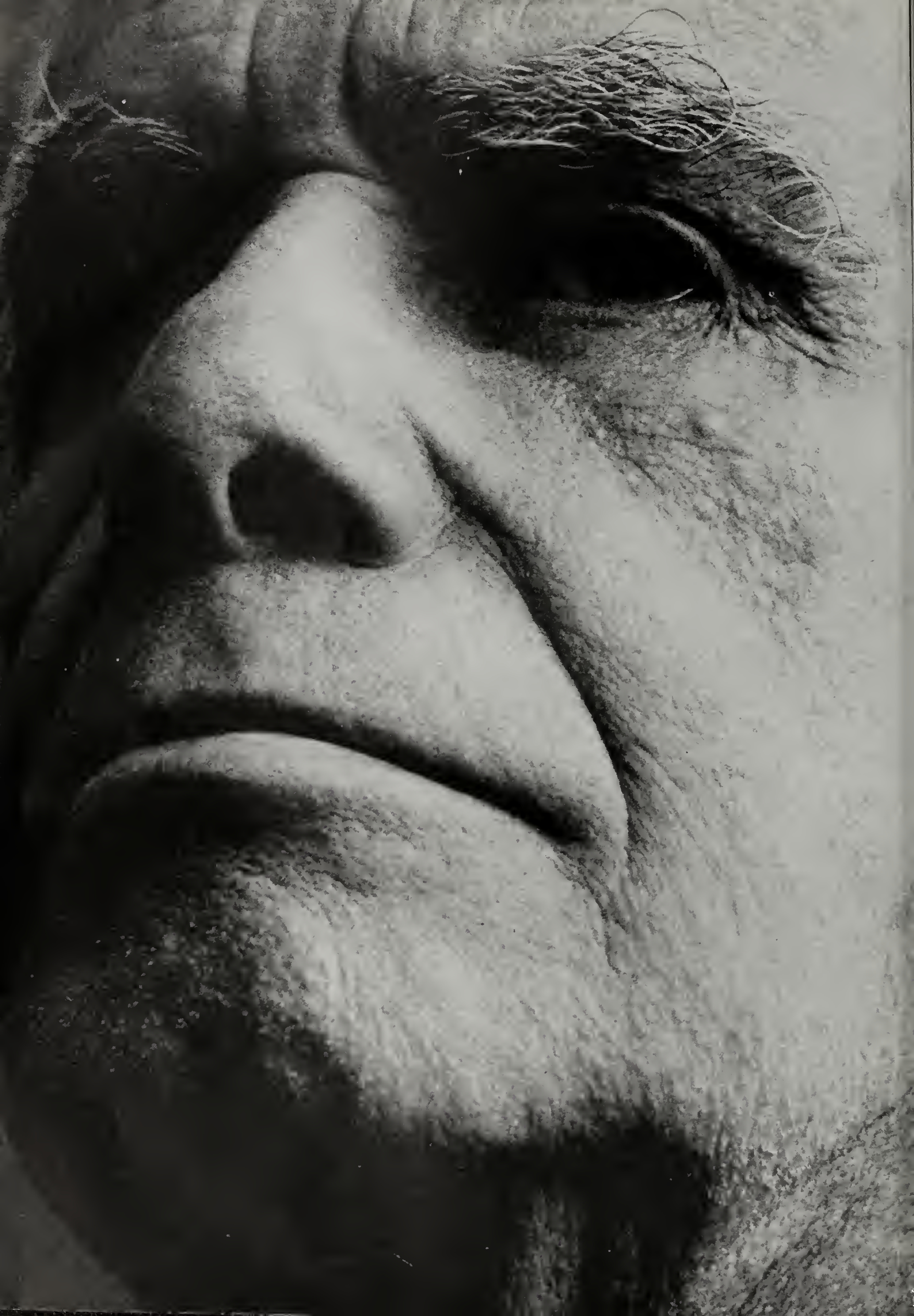

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Hydroxyzine has demonstrated its clinical effectiveness in the chemotherapeutic aspect of the total management of neuroses and emotional disturbances manifested by anxiety, tension, agitation, apprehension or confusion.

**Indications:** Total management in conditions of emotional stress requires in most instances a combined approach of psychotherapy and chemotherapy. Hydroxyzine has been found to be particularly useful for this latter phase of therapy in its ability to render the disturbed patient more approachable and amenable to psychotherapy in long-term treatment of the psychoneurotic and the psychotic, although it should not be used as the sole treatment of psychosis or of clearly demonstrated cases of depression.

Hydroxyzine is also useful in alleviating the manifestations of anxiety and tension in situations in which the causative stress is temporary, as in the preparation for dental and other minor surgical procedures, and in acute emotional problems. It has also been recommended for the management of anxiety associated with organic disturbances such as certain types of heart disease, digestive disorders, dermatoses, senility, the menopausal syndrome, and behavior problems in brain-damaged or epileptic children.

In addition, it has been recommended as adjunctive therapy in alcoholism, and allergic conditions with strong emotional overlay, as in asthma, chronic urticaria, and pruritus.

Hydroxyzine has also demonstrated effectiveness in controlling nausea and vomiting associated with gastritis, gastroenteritis and enteritis; upper respiratory infections, influenza and pneumonia; postoperative conditions; miscellaneous diseases such as Ménière's syndrome, migraine, and vestibulitis.

Hydroxyzine for intramuscular use is especially useful in treating the acutely disturbed or hysterical patient and the acute or chronic alcoholic patient with anxiety withdrawal symptoms or delirium tremens. Used adjunctively pre- and postoperatively and pre- and postpartum, hydroxyzine allays anxiety, permits substantial reduction in narcotic dosage and controls emesis.

Clinical use of hydroxyzine as an adjunct to the management of labor has been extensively reported in the literature without evidence of harm to the mother or fetus.

**Contraindications:** Hydroxyzine, when administered to the pregnant mouse, rat, and rabbit induced fetal abnormalities in the rat at doses substantially above the human therapeutic range. Clinical data in human beings are inadequate to establish safety in early pregnancy. Until such data are available, hydroxyzine is contraindicated in early pregnancy.

Hydroxyzine is contraindicated in any individual who has shown a previous hypersensitivity to it. The parenteral solution is intended only for intramuscular or intravenous administration and should not, under any circumstances, be injected subcutaneously or intra-arterially.

**Precautions:** Drowsiness may occur with oral or parenteral use of this drug, and patients should therefore be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Since hydroxyzine may potentiate the action of central nervous system depressants, conjunctive use with these drugs requires that their dosage be decreased. Hydroxyzine reduces the requirements by as much as 50% for narcotics such as meperidine, so their use in preanesthetic adjunctive therapy should be modified on an individual basis.

As with any preparation for intramuscular injection, Vistaril (hydroxyzine hydrochloride) Parenteral Solution should be injected well within the body of a relatively large muscle such as in the upper outer quadrant of the buttock or the lateral thigh. To avoid the possibility of radial nerve injury, injections should not be made into the lower and middle thirds of the upper arm. Aspiration and proper anatomical selection of injection site should be observed as a precaution against inadvertent injection into a blood vessel or major nerve. In a few instances of reported intravenous administration of hydroxyzine hydrochloride, digital gangrene has occurred distal to the injection site, apparently the result of endarteritis and thrombosis. This event has been considered due to inadvertent intra-arterial injection, although the possibility of periarterial extravasation, with arterial spasm, cannot be ruled out. Therefore, particular caution should be observed when hydroxyzine parenteral solution is administered intravenously to insure that it is injected only into intact veins; avoid either intra-arterial injection or extravasation. Due to infrequent phlebitis resulting from too rapid intravenous administration of the solution, the rate of injection should not exceed 25 mg. per minute. A single intravenous administration in excess of 100 mg. is not recommended (see Adverse Reactions).

**Adverse Reactions:** No serious side effects have been reported and confirmed in the administration of hydroxyzine to date. While therapeutic doses of hydroxyzine seldom produce impairment of mental alertness, transient drowsiness may occur; this may disappear in a few days of continued therapy or upon dosage reduction. Dryness of the mouth may be seen with higher doses. Involuntary motor activity, including rare instances of tremor and convulsions, has been reported, usually with doses considerably higher than those recommended. Extensive clinical use has substantiated the absence of toxic effects on the bone marrow or liver when hydroxyzine was administered in recommended doses for over four years of uninterrupted therapy.

When this product is given intravenously undiluted, minimal amounts of intravascular hemolysis occur at the site of injection. Giving the maximum recommended intravenous dose (100 mg.) to adults results in immediate transient hemolysis with the liberation of a total of 2-3 grams of hemoglobin, which, in some individuals, can cause small amounts of hemoglobinuria. (In the course of normal red cell destruction in the body, approximately 8 Gm. of hemoglobin are liberated every 24 hours.) Therefore, it is recommended that, when given intravenously, parenteral hy-

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*(Continued from preceding page.)*

droxyzine be diluted with 50 cc. of normal saline and given during a period of four minutes or more; with this technique, drug-induced hemolysis is unlikely.

Dosage: *Oral*—Adults: Dosage varies with individual requirements and ranges from 25 mg. t.i.d. to 100 mg. q.i.d.

Children: *under 6 years,* 50 mg. daily in divided doses; *over 6 years,* 50-100 mg. daily in divided doses.

*Parenteral*—For adult psychiatric and emotional emergencies, including acute alcoholism—I.M.: 50-100 mg. Stat., and q. 4-6 h., p.r.n.; I.V.: 50 mg. Stat., maintain with 25-50 mg. I.V. q. 4-6 h., p.r.n.

Nausea and vomiting—Adults: 25-100 mg. I.M. or I.V.; Children: 0.5 mg./lb. body weight I.M.

Pre- and postoperative adjunctive medication—Adults: 25-100 mg. I.M. or I.V.; Children: 0.5 mg./lb. body weight I.M.

Pre- and postpartum adjunctive therapy—25-100 mg. I.M. or I.V.

Patients may be started on parenteral therapy when indicated by the clinical situation. They should be maintained on oral therapy whenever this route is again practicable.

As with all potent medications, the dosage should be adjusted according to the patient's response to therapy.

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| Each cc. contains: | 25 mg./cc. | 50 mg./cc. |
|---|---|---|
| Hydroxyzine hydrochloride | 25 mg. | 50 mg. |
| Benzyl alcohol | 0.9% | 0.9% |
| Sodium hydroxide (approx.) to adjust to optimum pH | 0.22% | 0.46% |
| Water for Injection | q.s. | q.s. |

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## NATIONAL AND REGIONAL MEETINGS

**August 23–26: American Physiological Society. Howard University, Washington. Address: Dr. Ray G. Daggs, Executive Secretary, 9650 Rockville Pike, Bethesda, Md. 20014.**

**August 27–31: American Society for Pharmacology and Experimental Therapeutics. Howard University, Washington. Dr. Ellsworth B. Cook, Executive Secretary, 9650 Rockville Pike, Bethesda, Md. 20014.**

August 27–September 1: American Academy of Physical Medicine and Rehabilitation. Americana Hotel, Miami Beach, Fla. Address: Mr. Creston C. Herold, Executive Director, 30 North Michigan Avenue, Chicago, Ill. 60602.

**September 1–3: Society for Clinical and Experimental Hypnosis. Washington. Dr. Ericka Fromm, Executive Secretary, 5843 University, Chicago, Ill. 60637.**

September 7–9: American Association of Obstetricians and Gynecologists. The Homestead, Hot Springs, Va. Address: Dr. Robert B. Wilson, Secretary, 200 First Street, S.W., Rochester, Minn.

September 10–15: Flying Physicians Association. Williamsburg Inn, Williamsburg, Va. Address: Mr. Albert Carriere, 332 South Michigan Avenue, Chicago, Ill. 60614.

September 15–16: Tidewater Heart Association (8th Annual Cardiovascular Symposium). Golden Triangle Motor Hotel, Norfolk, Va. Address: Dr. Robert J. Robertson, Chairman, 523 Boush Street, Norfolk, Va. 23510.

September 18–21: American Academy of General Practice. Market Hall, Dallas. Address: Mr. Mac F. Cahal, Executive Director, Volker Blvd. at Brookside, Kansas City, Mo. 64112.

September 22–29: College of American Pathologists. Palmer House, Chicago. Address: Mr. Oliver J. Neibel, Jr., Executive Director, 230 North Michigan Avenue, Chicago, Ill. 60601.

September 22–30: American Society of Clinical Pathologists. Palmer House, Chicago. Address: Miss Martha Damron, Administrative Secretary, 445 North Lake Shore Drive, Chicago, Ill. 60611.

**September 25: Society for Pediatric Radiology. Washington Hilton Hotel, Washington. Address: Dr. John L. Gwinn, Secretary-Treasurer, Children's Hospital, 4614 Sunset Blvd., Los Angeles, Calif. 90027.**

September 25–26: 27th AMA Congress on Occupational Health. Regency Hyatt House, Atlanta, Ga. Address: Dr. Henry F. Howe, Director, Department of Occupational Health, AMA, 535 North Dearborn Street, Chicago, Ill. 60610.

**September 26–29: American Roentgen Ray Society. Washington Hilton Hotel, Washington. Address: Dr. Ted F. Leigh, Secretary, Emory University Clinic, Atlanta, Ga. 30322.**

**November 20–22: Annual Scientific Assembly, The Medical Society of the District of Columbia. Statler-Hilton Hotel, Washington. Address: Mr. George W. Cooley, Executive Director, 2007 Eye Street, N.W., Washington, D. C. 20006.**

# BOOKS RECEIVED

Acknowledgment is made of the following books which have recently been received.

**Current Concepts in Ophthalmology.** Bernard Becker, M.D., and Robert C. Drews, M.D. Price, $17.25. Pp. 265, with 127 illustrations. St. Louis: Mosby, 1967.

**Cecil-Loeb Textbook of Medicine,** 12th ed. Edited by Paul B. Beeson, M.D., and Walsh McDermott, M.D. Price, $20.50; 2-volume set, $24.50. Pp. 1738, illustrated. Philadelphia: Saunders, 1967.

**The Doctor Shortage: An Economic Diagnosis.** Brookings Studies in Social Economics. Rashi Fein. Price, $6.00; paper, $2.50. Pp. 199, illustrated. Washington, D.C.: Brookings Institution, 1967.

**Synopsis of Pediatrics,** 2nd ed. James G. Hughes, B.A., M.D., with 26 collaborators. Price, $10.85. Pp. 1099, with 86 illustrations. St. Louis: Mosby, 1967.

**The Neuroses.** Henry P. Laughlin, M.D. Price, $25.00. Pp. 1076. Washington: Butterworths, 1967 (distributed by Appleton-Century-Crofts).

**A Textbook for Medical Assistants.** M. Murray Lawton, M.D., and Donald F. Foy, B.S., M.S. Price, $8.85. Pp. 465, with 112 illustrations. St. Louis: Mosby, 1967.

**Pathology,** 3rd ed. Stanley L. Robbins, M.D. Price, $20.50; 2-volume set, $25.00. Pp. 1434, illustrated. Philadelphia: Saunders, 1967.

**Pathologic Physiology. Mechanisms of Disease,** 4th ed. William A. Sodeman, M.D., Sc.D., F.A.C.P., and William A. Sodeman, Jr., M.D. Price, $19.00. Pp. 1051, illustrated. Philadelphia: Saunders, 1967.

**Atlas of Intestinal Stomas.** Rupert B. Turnbull, Jr., M.D., F.A.C.S., and Frank L. Weakley, M.D. Price, $21.50. Pp. 207, with 182 illustrations by Robert M. Reed. St. Louis: Mosby, 1967.

**Ciba Foundation Study Group No. 25. Mongolism.** In Commemoration of Dr. John Langdon Haydon Down. Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Ruth Porter, M.R.C.P. Price, $3.50. Pp. 99, with 23 illustrations. Boston: Little, 1967.

**Ciba Foundation Study Group No. 26. Effects of External Stimuli on Reproduction.** In Honour of Professor B. Zondek. Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Maeve O'Connor, B.A. Price, $3.50. Pp. 107, with 10 illustrations. Boston: Little, 1967.

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VOLUME 36 • AUGUST 1967

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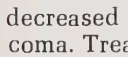

*Dosage:* 50-200 mg. (¾-3 grains) at bedtime.

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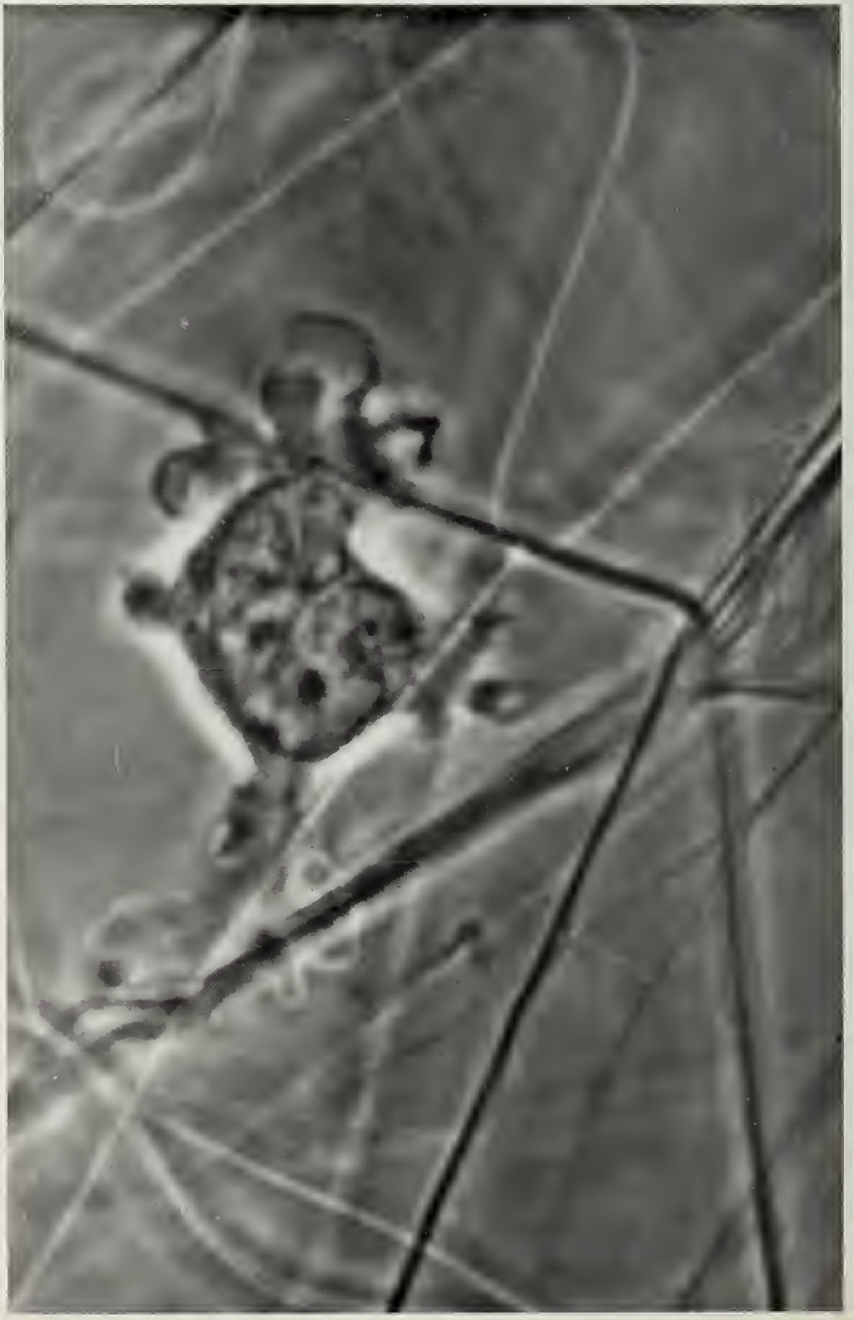
# INFLAMMATION:
# A cellular fight for life

*A SYNTEX REPORT based on recently developed hypotheses about topical corticosteroids, including the cellular theories of inflammation by Thomas F. Dougherty, Ph.D., University of Utah.*

You are looking at a fibroblast fighting for life. This cell—one of the most common found in connective tissue—has literally been poisoned by cytotoxins released from other cells that have ruptured. Soon, if the abnormal activity of this fibroblast does not cease, it, too, will rupture and die—one more casualty in the inflammatory wave of destruction precipitated by injury.

Until a short time ago no one had ever witnessed such a scene at the cellular level. Now, through advanced cinemicrographic techniques, it is possible to view and photograph the inflammatory process as produced experimentally in living animal tissue. This method permits new insight into the mechanism of inflammation and the role of corticosteroids in therapeutic management. Equally important, these techniques shed new light on factors that may make one corticosteroid more effective than another—factors that can be correlated with other chemical, biologic, and clinical parameters.

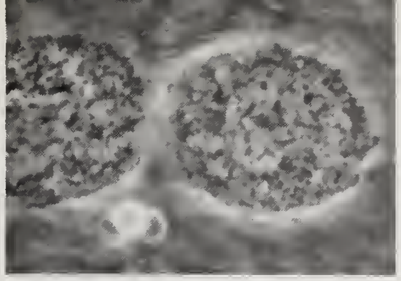


## Visual evidence of how corticosteroids influence the inflammatory reaction

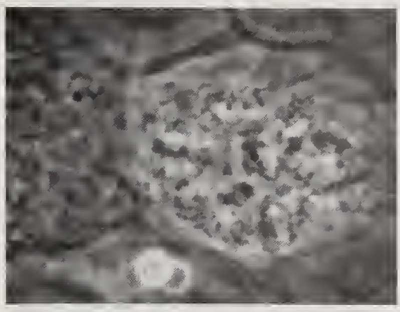
Working with phase-contrast cinemicrography on living animal tissue, Doctors Thomas F. Dougherty and David Berliner of the University of Utah College of Medicine have actually filmed cellular events that occur during the inflammatory reaction. This remarkable study* and additional work by these investigators, as well as by others, have established a new theoretical biologic basis for the antiinflammatory effect of the corticosteroids. (It must be noted that other theories, such as the lysosome or so-called "suicide bag" theory, have been postulated, although it is quite likely that there are more similarities than differences among the various theoretical models.)

## The inflammatory wave of destruction

In this investigation an injurious injection of gelatin is used to set off an inflammatory reaction in living mouse tissue. What follows is a wave of destructive cellular activity that comprises the inflammatory response to injury. Mast cells (which contain heparin, serotonin and histamine) take up water, swell and rupture, releasing their contents, which are toxic outside the mast cell wall. These toxins, in turn, cause disintegration of other cells (such as fibroblasts) and the release of additional toxic material. Capillaries, too, take up water and leak unformed blood elements, causing edema. And polymorphonuclears, lymphocytes and perithelial cells invade the inflamed site. As a result of all these changes, the cellular environment reaches a state of turmoil.



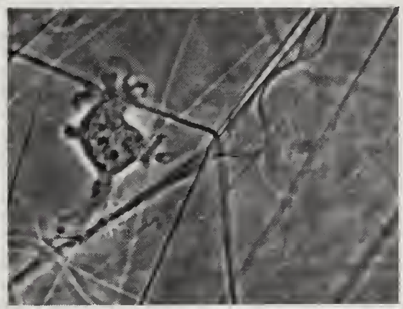
*Phase-contrast microscopy showing mast cell before injury.*



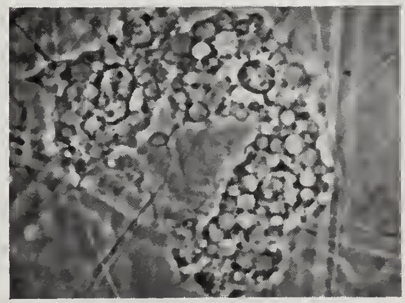
*Mast cell (after injury) has broken up and released cytotoxins.*

## How corticosteroids change the picture

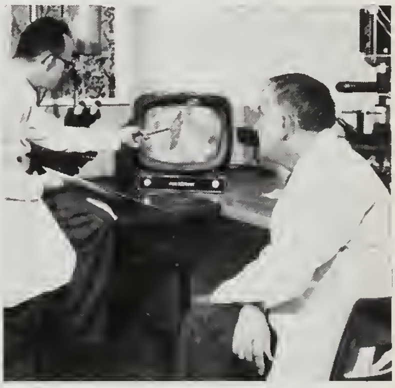
Corticosteroids appear to virtually stop the abnormal cellular activity that constitutes the inflammatory reaction. This permits the body's natural resources to clear up the inflamed area and repair the damaged tissue. This interpretation is supported by the fact that when the injurious gelatin solution is injected simultaneously with a corticosteroid – Synalar (fluocinolone acetonide) – the inflammatory pattern simply does not develop.



*Fibroblast in high state of activity, much distorted.*



*Mast cells showing effects of corticosteroid action: cells are normal in size, shape and activity.*



In summarizing his study Doctor Dougherty states: "...we also feel this work may explain why one corticosteroid helps a patient more rapidly and effectively than another. If it does, it is because one corticosteroid is the fastest, most effective inhibitor of the series of inflammatory events at the tissue level."

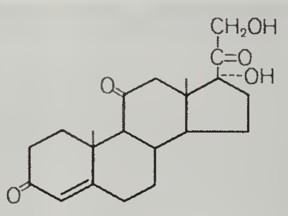
---

**A New View of Corticosteroid Action in Inflammatory Dermatoses*, a film based on this study, is now available from your Syntex representative.

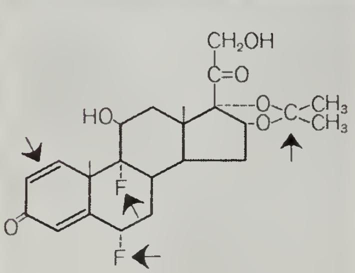
*See last page for*

# How advances in chemical design have achieved greater steroid potency

The chemical modification of corticosteroid molecules from the advent of hydrocortisone to the development of Synalar (fluocinolone acetonide) is a prime example of how biochemists can "design" to increase therapeutic activity and minimize undesirable side actions. Below, for example, we see the important changes that were made in reference to the hydrocortisone molecule to produce fluocinolone acetonide, one of the most active of all topical corticosteroids. As a result, a 0.01% preparation of Synalar (fluocinolone acetonide) has been reported to do the work of a 1% hydrocortisone product containing 100 times more cortiscosteroid. And it can often do it more effectively.



**Hydrocortisone**

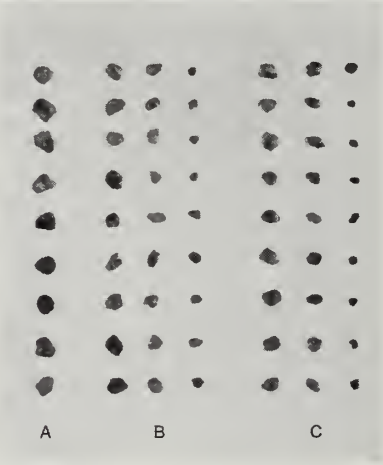


**Fluocinolone Acetonide (Synalar)**

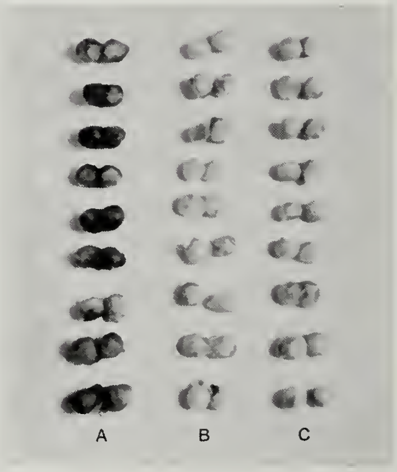
- ☐ *a double bond between carbons 1 and 2*
- ☐ *fluorine substitutions at both the 6-α, and the 9-α positions*
- ☐ *the addition of the acetonide at the 16-α. 17-α positions, thus providing one of the most potent topical corticosteroids available.*

### How bioassay tests are used to "predict" therapeutic potential

Biologic assays are another tool used by researchers to help establish the relative activity of corticosteroids. To date no single method of assaying corticosteroid activity has emerged as the ideal "yardstick" for predicting therapeutic potential. Taken together, however, these methods have proved useful. When such tests are run on various corticosteroids, a definite order of corticosteroid activity becomes evident. Compounds with the highest order of activity may be expected to merit clinical trial to establish their high therapeutic potential. When assayed by these methods, fluocinolone acetonide (Synalar) emerges as one of the most active topical corticosteroids, milligram for milligram, available for clinical application today.



The Thymus Involution Assay[1-4] is run on adrenalectomized rats. The sizes of the glands are measured, and the degree of involution caused by the steroid is determined as an indication of its potency. In the above photo, the comparative involution of thymus glands achieved with hydrocortisone and Synalar (fluocinolone acetonide) is shown. Untreated controls (A) show normal size. Group B – injected with 1, 2 and 4 mg. of hydrocortisone – show progressively smaller thymuses as does Group C – injected with fluocinolone acetonide – but with only 1/500th the dose of hydrocortisone.



The Antigranuloma Assay[1-4] also utilizes adrenalectomized rats. Granulomas are induced by subcutaneous implantation of cotton pellets on either side of the thorax. The degree of granuloma inhibition achieved by a steroid reflects its potency. The above photo shows the inhibition of granuloma formation achieved with hydrocortisone and Synalar (fluocinolone acetonide). Untreated controls (A) show large, red granulomas adhering to the pellets. Group B, receiving hydrocortisone and Group C, receiving fluocinolone acetonide, show little, if any, granuloma formation. Fluocinolone acetonide produced the same effect as hydrocortisone with only 1/500th the dose. This assay, as well as the thymus involution assay, measures systemic rather than topical corticosteroid activity. Nevertheless, results by these methods correlate well with other assays and with the milligram potencies of topical steroids in current clinical use.

# Worldwide clinical experience confirms the predictable therapeutic potential of Synalar

It is particularly gratifying that the promise of the advanced chemical design and high order of bioassay activity of Synalar (fluocinolone acetonide) has been confirmed by widespread therapeutic application. Indeed, the impressive clinical response rate of Synalar has been documented in no fewer than 232 papers from 22 countries.

## Representative Clinical Results with Synalar*

### Efficacy Documented in over 4,000 Patients

| Condition | Number of Publications | Number of Patients | Significant Improvement† |
|---|---|---|---|
| Contact Dermatitis | 27 | 750 | 713 |
| Eczematous Dermatitis | 21 | 472 | 409 |
| Seborrheic Dermatitis | 18 | 442 | 426 |
| Atopic Dermatitis | 24 | 460 | 426 |
| Psoriasis | 36 | 1,699 | 1,510 |
| Neurodermatitis | 18 | 351 | 324 |
| Total | 144 | 4,174 | 3,808 |

*Complete bibliography on request.

†Expressed by the authors as excellent, very good, good, complete remission of inflammation, etc.

PRESCRIBING INFORMATION *For initiation of therapy:* Cream 0.025%, 5 and 15 Gm. tubes, 425 Gm. jars; *for emollient effect:* Ointment 0.025%, 15 Gm. tubes; *for maintenance therapy:* Cream 0.01%, 15 and 45 Gm. tubes, 120 Gm. jars; *for intertriginous or hairy sites:* Solution 0.01%, 20 cc. and 60 cc. plastic squeeze bottles; *for infected inflammatory dermatoses:* Neo-Synalar® Cream (0.025% fluocinolone acetonide, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes. CONTRAINDICATIONS: Tuberculous, fungal, and most viral lesions of the skin, (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. PRECAUTIONS: Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. When severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. SIDE EFFECTS: Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. The neomycin in Neo-Synalar Cream rarely produces allergic reactions.

REFERENCES: 1. Lerner, L. J., Bianchi, A., Turkheimer, A. R., Singer, F. M., and Borman, A.: Anti-inflammatory steroids: potency, duration and modification of activities. Ann NY Acad Sci 116:1071 (Aug. 27) 1964. 2. Idem: Comparison of anti-granuloma, thymolytic and glucocorticoid activities of anti-inflammatory steroids. Proc Soc Exp Biol Med 116:385 (June) 1964. 3. Ringler, A.: Activities of adrenocorticosteroids in experimental animals and man, in Dorfman, R. I.: Methods of hormone research, New York, Academic Press, 1964. vol. III. pp. 234-280. 4. Gubersky, V. R.: To be published.

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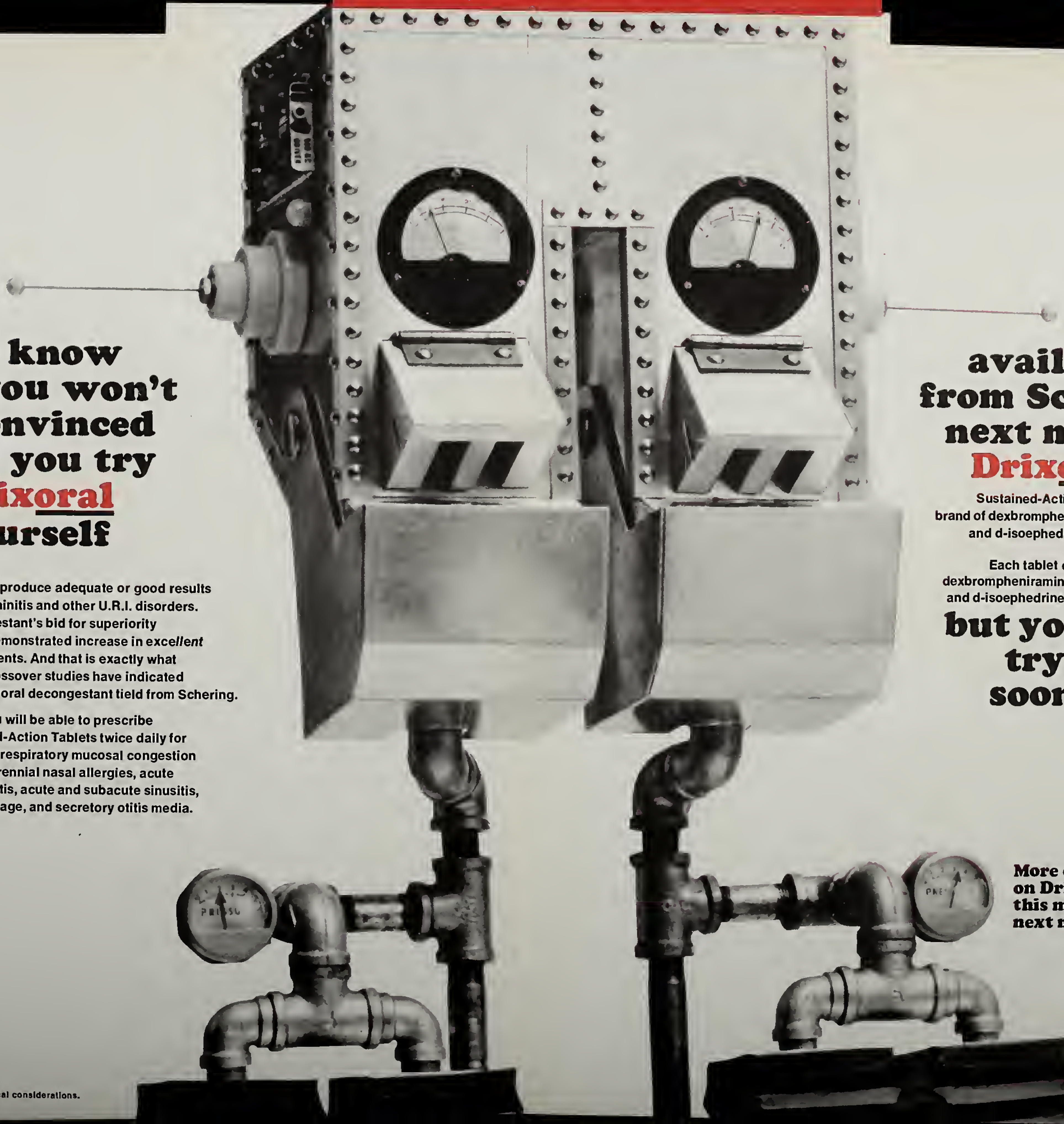

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References:
1. Pullen, F. W. 2nd, and Montgomery, W. W.: Arch. Otolaryng. 77:24, 1963.
2. Frank, D. I.: Curr. Therap. Res. 6:158, 1964.
3. Fierberg, A. A.: Ann. Allergy 22:324, 1964.

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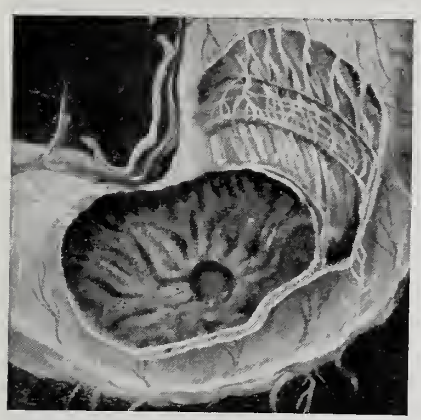

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*of the District of Columbia*

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## Columbia Hospital for Women Number

THIS SPECIAL ISSUE of the MEDICAL ANNALS commemorates more than a century of devoted public service by Columbia Hospital for Women. For the COLUMBIA HOSPITAL FOR WOMEN NUMBER the Editorial Board is indebted to Dr. Franklin Hodge, Chairman, and the members of his committee, Drs. William J. Jaffurs, Jed W. Pearson, Jr., and Violet Bowen Hugh, who secured from the hospital staff the papers which appear in this issue.

# Diagnosis of Carcinoma of the Cervix Uteri in Pregnancy

JORGE E. MEDINA, M.D.,* THOMAS R. TURNER,† IN WHAN CHANG, M.D.,‡ JAI YEOUNG AHN, M.D.,§
ALBERTO FORTUNY, M.D.,‖ DAVID A. KUSHNER, M.D., F.A.C.S., F.A.C.O.G.,¶
AND WILLIAM J. JAFFURS, M.D.#

THE DIAGNOSIS of cervical cancer in the pregnant woman must be established through a carefully planned study. It should be accomplished with little or no adverse effect to the pregnancy. Two lives are at risk, those of the mother and the fetus. Through the years exfoliative cytology has been utilized as an effective cancer-screening aid in the nonpregnant female. It is only in recent years that pregnant women have been subjected to routine cytology examination with increasing success,[1-4] yet tissue examination remains the only reliable means by which diagnosis of the kind of lesion of the cervix can be made. The challenge is to perform the proper diagnostic procedure only on those who are suspect for cancer of the cervix. These women must be detected either through a thorough pelvic examination which reveals an abnormal cervix or by study of the exfoliated cells from the vagina and cervix. Cytology studies in our hospital before 1962 were made only on gynecologic patients and a selected group of obstetrical patients with suspected lesions. Since then our aim has been to perform a cytologic examination in all pregnant women and to submit the "suspect patient" to a planned step-by-step study in which the cancer diagnosis is finally established by tissue examination.

## Methods and Materials

All 5,787 patients registered in the Prenatal Clinic at Columbia Hospital for Women in Washington, D. C. were studied from July 1, 1962 through June 30, 1966. The population study was composed of 15 per cent white and 85

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per cent nonwhite patients. At least 2 cytologic examinations were performed on each patient, one at the first prenatal visit and the other at the postpartum visit. The Riva-Turner acridine-orange (10-second stain) technique and rapid screening method was utilized as the laboratory method of choice. This method has been described and reported by one of us.[5,6]

At the time of diagnostic surgery a Schiller's test was usually performed. Multiple punch biopsies and/or cold knife conization specimens were taken during the prenatal and postpartum periods for tissue diagnosis.

The carcinoma in situ lesions were treated by the accepted conventional hysterectomy with preservation of at least 1 ovary. Several patients were permitted to preserve their fertility state for at least another pregnancy. There were no cases of invasive disease discovered before delivery which required radical treatment. The invasive cancer discovered in the postpartum period was treated by the radical Wertheim surgical procedure. Each microinvasive lesion was treated differently, one by the Schauta-Amreich operation and the other by extended abdominal hysterectomy. In both patients the adnexa were preserved.

### Results

Table 1 summarizes our findings in the 5,787 patients studied over the 4-year period. The first year was considered a prevalence study year. The second, third and fourth year studies are not true incidence studies since only a majority and not all of the patients continued to attend the outpatient clinic in subsequent pregnancies. No correction to determine the true incidence in the study population has been attempted. All of these patients' smears were classified as suspicious on the basis of the morphologic abnormalities of the cells. This classification corresponds to Papanicolaou class III. No class V cases were discovered. Repeated cytologic examinations performed in all patients with suspicious smears reverted to normal limits in 19 patients following local anti-inflammatory treatment with Tricofuron.* Six patients were lost in the follow-up study. In 3 patients transferred to other hospitals outside of the Washington Metropolitan Area during the period of study the tissue diagnosis was not established in 2.

**TABLE 1: Incidence of Lesions in 5,787 Patients by Years**

| | 1962–1963* | 1963–1964 | 1964–1965 | 1965–1966 | bined |
|---|---|---|---|---|---|
| Pregnant patients screened | 1,472 | 1,134 | 1,580 | 1,601 | 5,787 |
| Suspicious cells (initial) | 26 | 10 | 13 | 18 | 67 |
| Suspicious cells (confirmed) | 23 | 8 | 6 | 11 | 48 |
| Chronic cervicitis, severe | 0 | 0 | 1 | 2 | 3 |
| Dysplasia, cervix | 12 | 4 | 4 | 3 | 23 |
| Carcinoma in situ, cervix | 8 | 3 | 1 | 4 | 16 |
| Microinvasive carcinoma | 2 | 0 | 0 | 0 | 2 |
| Invasive carcinoma | 1 | 0 | 0 | 0 | 1 |
| Patients lost to study | 0 | 1 | 1 | 4 | 6 |

* 1962–1963: First-year study of prevalence in clinic patients.

The majority of the patients were registered in the clinic during the second and third trimesters. Four patients with abnormal cells were discovered during the first trimester, 21 during the second, and 34 during the third. Eight patients did not present themselves for a prenatal visit, and subsequent to their delivery the first smear examination was obtained at the first postpartum visit.

The average age of patients with suspicious cells was 26.1 years; the youngest patient was 17 years of age and the oldest 43. In the carcinoma-in-situ group, the average age was 30.6 years. Comparison of the gravidity and parity of the carcinoma-in-situ group with the suspicious group of patients showed that the former had more pregnancies, 6.6, and infants, 5.4, than did the latter group, 4.3 and 3.8, respectively. Two patients, ages 24 and 25 years, had microinvasive carcinoma. One patient had invasive carcinoma at the age of 33 years. The last 2 groups are considered to be of little statistical value because of the small number of cases.

Tissue was obtained for pathologic diagnosis in 45 patients. The suspicious cells in smears from 42 patients correlated either with dysplasia or cervical cancer. There were 3 instances of severe erosive cervicitis diagnosed. The pathologic diagnosis was established on tissue examination in 28 patients before delivery. Later, 11 of the patients with dysplasia as the tissue diagnosis exhibited negative cytology findings after delivery. No further biopsy examination was performed, and the patients subsequently were followed by smears alone as part of the incidence study. Nine of 28 patients in whom the pathologic diagnosis had been established during pregnancy had repeated biopsy procedures after delivery for additional study to confirm the prenatal tissue diagnosis. Seventeen of the 45 patients were operated upon and studied by tissue examination in the postpartum period.

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* Tricofuron, a product of Eaton Laboratories, Norwich, N.Y.

More specifically, in the group of patients with cancer diagnostic surgery was performed on 13 during the prenatal period. Nine were diagnosed as having carcinoma in situ, and 4 exhibited dysplastic lesions. Suspicious cells persisted, and repeated conization and/or hysterectomy postpartum revealed intra-epithelial carcinoma in all. Six patients of this same cancer group did not have diagnostic surgery before delivery for several reasons. Cytologic examination on one patient was done a day before delivery and biopsy postpartum. Another patient had abnormal cell findings after admission for incomplete abortion; 2 patients were lost to follow-up but returned later after delivery for further studies.

## Discussion

The management of the pregnant patient with an abnormal cervix presents certain difficulties in diagnosis. The surgical procedures involve a number of complications which may be immediate or delayed. Immediately they may produce abortion or premature labor; later there may be interference with the normal dilatation of the cervix at the time of labor and cervical laceration at the time of delivery. Two other important complications are hemorrhage and the postoperative infection. Many obstetricians still believe that the aggressive surgical approach in the pathologic diagnosis of the cervix in pregnancy is contraindicated because of these infrequent complications. We are of the opinion that the patient must be investigated and a definitive diagnosis established despite the chances of these complications. It is far more advantageous to diagnose and treat an early carcinoma than an advanced cancer.[7]

We follow a sequence of progressive steps beginning with the routine cytologic examination of all pregnant women in our prenatal clinic. Further, we investigate those patients who present doubtful clinical changes in their cervix as well as those in whom suspicious (class III or higher) cytology has been reported. All patients with abnormal cells have a second examination in 2 weeks after local treatment for any inflammatory condition (trichomoniasis, moniliasis, etc.) that may be present. If the repeated examination is negative the patient is followed by exfoliative cytologic examination throughout her pregnancy and in the postpartum period. No further diagnostic procedure is considered unless the smear should become suspicious. If the second examination remains suspicious (class III or higher) we firmly believe that diagnostic procedures should be performed regardless of the stage of pregnancy. We employ the Schiller's test prior to diagnostic surgery. Although the Schiller's test is not specific for cancer it is a helpful aid in pinpointing the abnormal suspicious areas for biopsy either in the office, prenatal clinic, or operating room.[8] Biopsy specimens from the 4 quadrants of the cervix plus all Schiller positive areas are taken. None of the patients suffered postoperative hemorrhage or infection following the punch biopsies. Local therapy after the surgery was accomplished through the use of antibiotic vaginal cream.* If the tissue examination is benign we repeat the cytologic examination in 4 weeks. If the second examination is again negative we continue to follow the patient throughout her pregnancy and postpartum by this simple means. If the tissue examination reveals invasive cancer the pregnant patient is treated according to the clinical stage of the cancer and the period of gestation.

If the biopsy specimen is diagnosed as dysplasia or carcinoma in situ we believe that conization is an acceptable means for definitive diagnosis. Conization is employed in every possible instance. Only 1 of our patients had to be readmitted after conization because of bleeding, and this was controlled with vaginal packing.

An equally important aspect of the study program is careful reëxamination of all patients in the postpartum period. If for the first time the cytologic examination reveals suspicious cells, a complete diagnostic work-up is done. If no residual cancer is discovered the patient may continue under surveillance if she desires further pregnancies. Hysterectomy for in situ cancer of the cervix is recommended if the patient no longer desires further childbearing.

It is extremely important to reassess the pathologic process in the cervix prior to any definitive therapy. In situ cancer or the premalignant lesions of the cervix may take various pathways in their development during pregnancy. We have considered them from 3 different aspects.

1. *The lesion discovered during pregnancy may persist unchanged throughout the period of gestation.* The persistence of the cancer in situ during pregnancy was first reported by Marsh and Fitzgerald[9] in 1956. Additional studies by other investigators have confirmed this phenomenon.[10, 11, 12] Richart[13] in 1963 followed 42 pregnant patients with a

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* Furacin Vaginal Cream, a product of Eaton Laboratories.

diagnosis of dysplasia or carcinoma in situ by means of cytologic examination and colpomicroscopy without biopsy. He reported that no regression was noted in the original lesions.

2. *The lesion discovered during pregnancy is no longer found to be present in the cervix.* The lesion may have been removed by multiple punch biopsies or by conization performed during pregnancy. Takeuchi and McKay[14] reported in their series of 20 cases that the area of cervix involved by carcinoma in situ showed a mean area of 0.25 sq. cm., whereas that for anaplasia (dysplasia) alone was 0.93. The combined area for carcinoma in situ plus anaplasia (dysplasia) was 1.51 sq. cm. This is not a large area of involvement. We feel that small early lesions may be included within the boundaries of the biopsy or the conization specimen at diagnostic surgery. Other investigators have thought that there is a true spontaneous regression of the lesion after delivery.[15, 16] This has also been reported in nonpregnant patients by McKay[17] in whom he found 20 per cent of the dysplastic lesions to show a spontaneous disappearance on careful follow-up examination.

**TABLE 2: Summary of Management of Nineteen Pregnant Women with Cancer of the Cervix**

| Case | Antepartum | | | | | Postpartum | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cytology* | | | Punch Biopsies | Conization | Cytology | | | Punch Biopsies | Conization | Treatment† | Remarks | Cytology Follow-up |
| | 1st | 2nd | 3rd | | | 1st | 2nd | 3rd | | | | | |
| 1 | A | S | HS | Dysplasia | — | | | | CA in situ | CA in situ | T.A.H. | No residual CA | N |
| 2 | N | S | | — | — | HS | S | | — | CA in situ | T.A.H. | No residual CA | N |
| 3 | S | S | | Dysplasia | Dysplasia | S | S | S | — | Dysplasia | T.A.H. | CA in situ | N |
| 4 | S | S | | Dysplasia | Dysplasia | S | S | | Dysplasia | — | T.A.H. | CA in situ | |
| 5 | S | A | | CA in situ | CA in situ | N | S | S | — | — | T.A.H. | No residual CA | |
| 6 | S | S | | — | — | S | | | — | CA in situ | T.A.H. | No residual CA | N |
| 7 | S | | | — | — | S | | | CA in situ | Invasive CA | R.W.H. | No residual CA | N |
| 8 | A | | | — | — | S | S | | — | CA in situ | T.A.H. | CA in situ | |
| 9 | S | HS | | — | Dysplasia | S | | | CA in situ | Microscopic invasive CA | E.A.H. | No residual CA | N |
| 10 | S | S | | CA in situ | — | A | | | Dysplasia | | | Patient refused conization | N |
| 11 | S | | | — | — | S | | | Microscopic invasive CA | Microscopic invasive CA | S-A.V.H. | No residual CA | N |
| 12 | S | | | — | CA in situ | | | | | | | Lost to follow-up | |
| 13 | HS | | | Abortion | | S | | | Dysplasia | CA in situ | Deferred | Pregnancy desired | N |
| 14 | S | S | | CA in situ | CA in situ | | | | | | C.H. | No residual CA | N |
| 15 | S | S | | — | CA in situ | | | | — | — | T.A.H. | Residual CA in situ | N |
| 16 | S | S | | CA in situ | | S | | | — | CA in situ | T.A.H. and L.S.O. | No residual CA | N |
| 17 | S | S | | — | CA in situ | N | | | — | — | Deferred | Pregnancy desired | N |
| 18 | S | S | | CA in situ | CA in situ | | | | — | — | T.A.H. and L.S.O. | No residual CA; ectopic pregnancy | N |
| 19 | S | S | | — | CA in situ | A | N | N | — | — | Deferred | Pregnancy desired | N |

* N = Negative
A = Atypical
S = Suspicious
HS = Highly suspicious

† T.A.H. = Total abdominal hysterectomy
R.W.H. = Radical Wertheim hysterectomy
E.A.H. = Extended abdominal hysterectomy
S-A.V.H. = Schauta-Amreich vaginal hysterectomy
C.H. = Cesarean hysterectomy
L.S.O. = Left salpingo-oöphorectomy

3. *The lesion may progress during the pregnancy and be far more serious postpartum.* Different investigators have demonstrated the progress of dysplasia to carcinoma in situ in from 2 to 4 per cent of all cases studied.[18, 19] The original lesion may not have been included within the area of biopsy or even conization before delivery, thereby permitting further growth from the tumor. This is particularly true in multiparas at the end of the last trimester when the internal os begins to dilate making it more difficult to obtain an adequate cone specimen. Again, the lesion may be multifocal or be present predominantly within the endocervix. In our unpublished experience[20] dealing with nonpregnant patients 10 per cent of the early cases of cancer of the cervix arose well within the endocervix and not at the squamocolumnar junction.

Several of our cases were considered to illustrate all of these important aspects of behavior concerning the persistence, regression, disappearance, or progression of the in situ lesion during pregnancy. Intra-epithelial carcinoma was discovered later postpartum in 4 patients who had an original diagnosis of dysplasia prior to delivery (cases 1, 3, 4 and 9—table 2). The patients of cases 3 and 4 demonstrated very clearly the value of repeated cytologic examination. Dysplasia was established in both cases during pregnancy by punch biopsies and confirmed by conization. Suspicious cells persisted after delivery and even after repeated diagnostic surgery in the postpartum period. On the basis of the persistent suspicious cytology report which was not explained by the tissue diagnosis of a persistent dysplasia, simple hysterectomy was performed in both cases, and a small focus of intra-epithelial carcinoma was discovered in the operative specimen. Patient 7 (table 2) revealed an invasive carcinoma by conization after the diagnosis of intra-epithelial carcinoma was made by punch biopsies. This is evidence for the reassessment of all patients prior to definitive therapy after their delivery.

## Conclusions

Exfoliative cytology is the best and most effective means for cervical cancer screening of patients during pregnancy.

Punch biopsy of a clinical lesion or a positive Schiller's area is of definitive value in the diagnosis of cancer of the cervix.

Conization is an acceptable means to establish the definitive diagnosis of intra-epithelial carcinoma.

All patients should be reassessed again during the postpartum period as part of the continuing cancer-screening program.

The rewards of the diagnosis of cervical cancer in pregnancy outweigh the risks from the diagnostic procedures.

Exfoliative cytology is an effective means for following patients who have in situ cancer or a premalignant lesion but wish to maintain their fertility.

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## R. N.'s Return

A refresher program designed to bring inactive registered nurses back into nursing is currently in progress in the Metropolitan Washington Area. Four courses have already been conducted at Alexandria Hospital, Sibley Memorial Hospital, and Washington Hospital Center, and 12 more are scheduled at various hospitals in Maryland, Virginia, and Washington, D. C.

The refresher course provides an opportunity for the inactive professional nurse to review and update her nursing knowledge and skills. Through 6 weeks of classroom lectures and discussions and supervised clinical practice the nurse can be guided to develop confidence in providing nursing care.

The majority of nurses who take the refresher course return to work part time at first, but later, as their children grow older, work on a full-time basis. These returning nurses are housewives as well as mothers who have been inactive in nursing from 1 to 30 years and range in age from 35 to 60.

The courses, made possible through funds granted under the Manpower Development and Training Act, are being offered to the registered nurse free of charge. The Hospital Council of the National Capital Area, Inc. and its 26 member hospitals are conducting the program. Mr. Gilbert Smith, Educational Coördinator, anticipates that approximately 325 inactive nurses will complete refresher courses and that 300 of these will return to professional nursing.

# Cytogenetic Studies in Patients with Developmental Sexual Deficiencies[*]

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Cytogenetic studies of patients with anomalous sexual development have proven extremely valuable to the clinician. Developmental anomalies to be considered in the prepuberal patient are those expressed predominantly at an anatomic level and are usually observed shortly after birth. Gross abnormalities are invariably detected early in life, whereas minor aberrations may not become apparent until after puberty. It has been our experience that the postpuberal patient most frequently seeks advice due to failure in the development of secondary sex characteristics, failure to establish normal menstrual pattern, or inadequate reproductive fitness, particularly sterility. It is not uncommon that the patient may have various combinations of the defects.

Anomalous sexual development has been a subject of study in the Cytogenetic Research Laboratory at the Columbia Hospital for Women. The findings over a 2-year period are summarized in this report. A total of 36 patients were studied and are summarized in table 1.

**TABLE 1: Developmental Sexual Deficiencies of Thirty-six Patients**

| Clinical Diagnosis | Prepuberal | Postpuberal | Age Range |
|---|---|---|---|
| Ambiguous external genitalia | 7 | | Newborn–2 years |
| Primary amenorrhea | | 9 | 16–34 years |
| Secondary amenorrhea | | 11 | 16–33 years |
| Primary oligomenorrhea | | 9 | 16–30 years |
| Totals | 7 | 29 | |

## Methods

Sex chromatin studies were done on duplicate buccal and/or vaginal smears. Samples were taken bilaterally, immediately fixed in ether-ethanol (95 per cent), and stained with cresylecht violet according to the method described by Ferguson-Smith.[1] In some cases sex chromatin was determined in tissue sections stained with routine hematoxylin-eosin.[2] Chromosomal analysis was done on cells from peripheral blood culture according to the method of Moorehead et al[3] as modified by Jacobson.[4] A minimum of 20 metaphase plates were subjected to analysis in each case.

## Results

*Prepuberal group.* Chromosomal analysis of the 7 patients with ambiguous external genitalia are shown in table 2. Gonadal sections were available for study in only 2 cases (case reports 1 and 2). In case 1 attempts to culture several tissues for chromosomal analysis were not satisfactory, and poor results were obtained in case 2 at another laboratory.

*Postpuberal group.* The 9 patients having primary amenorrhea yielded the greatest number of chromosomal aberrations. The summarized results are shown in table 3.

All of the patients in whom X-monosomy was found showed phenotypical characteristics of Turner's syndrome, i.e., short stature, cubitus

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**TABLE 2: Chromosomal Analysis in Patients with Ambiguous External Genitalia**

| Patient Code | Age | Anatomic Diagnosis | Sex Chromatin Body | Karyotype |
|---|---|---|---|---|
| C-6428 | Newborn | Enlarged clitoris; opening inferior to the phallus and connecting to the bladder; unfused scrotal sacs | Negative | Unsatisfactory |
| C-6535 | Newborn | Marked hypospadias; palpable testes on right | Negative | 46(XY) |
| C-6512 | 2 years | Enlarged clitoris; fused labia | Positive | 46(XX) |
| C-6542 | Newborn | Hypospadias; palpable testes; webbed toes | Negative | 46(XY) |
| C-6556 | Newborn | Fused labia or bifid scrotum; complete hypospadias; rudimentary glans or hypertrophy of clitoris | Negative | 46(XY) |
| C-6552 | Newborn | Hypertrophy of clitoris and labia minora; labia majora as scrotal sac; small vaginal opening | Positive | 46(XX) |
| P-64150 | Newborn | Hypertrophy of clitoris and labia majora; webbed neck; micrognathia; microglossia; cleft palate; extra digits and toes | Negative | 46(XO)/47(XY) |

**TABLE 3: Chromosomal Analysis in Patients with Primary Amenorrhea**

| Patient Code | Age in Years | Height | Sex Chromatin Body | Karyotype |
|---|---|---|---|---|
| C-65-6 | 31 | 4'11" | Negative | 45(XO) |
| C-64-46 | 21 | 4'11" | Negative | 45(XO) |
| C-65-4 | 21 | 5'2" | Positive | 46(XX) |
| C-65-5 | 33 | 4'11½" | Negative | 45(XO) |
| C-65-6 | 34 | 5'1½" | Positive | 46(XX) |
| C-65-11 | 32 | 4'11" | Negative | 45(XO) |
| C-65-24 | 23 | 4'11" | Positive | 46(XX) |
| H-66-681 | 27 | 5'8" | Negative | 46(XY) |
| C-666 | 17 | 5'10" | Double positive | 47(XXX) |

valgus, shield chest, low hair line, poor breast development, scant pubic hair, and infantile external genitalia. Webbing of the neck, however, was absent in 1 case and almost imperceptible in another. Breast development had somewhat improved in 2 of the patients following earlier estrogen therapy. Endocrine studies were not systematically done by all of the referring physicians. The diagnostic tests performed in 5 of these patients are summarized in table 4.

Three patients (table 3) showed no chromosomal basis for their amenorrhea. Two of these had other positive findings which helped to explain their menstrual failure, and the third was referred for further endocrine evaluation. Patient C-65-6 had undergone brain surgery at the age of 11 years for blockage of the aqueduct of Sylvius. Culdoscopy revealed tiny bilateral ovarian structures. Another patient, C-65-24, had polycystic ovaries for which wedge resection was recommended.

The 11 patients who had secondary amenorrhea were unusual in that the majority had never established a regular menstrual pattern. However, secondary sex characteristics were considered within normal limits in all 11. The average stature was well above that of the group of patients with primary amenorrhea. Chromosomal analysis disclosed 1 abnormal case with the mosaic pattern

**TABLE 4: Endocrine Studies in Patients with Primary Amenorrhea**

| Patient Code | Age in Years | Sex Chromatin Body | Karyotype | 17-keto-steroids mg./24 hr. | P.B.I. mcg. % | Urinary Estrogen mcg. % | Gonadotrophins* | Skull X-rays |
|---|---|---|---|---|---|---|---|---|
| C-64-46 | 21 | Negative | 45(XO) | 16.2 | 4.7 | 91<br>127 | 9 R.U. | Normal |
| C-65-4 | 21 | Positive | 46(XX) | 18.7 | 5.0 | | 28 R.U. | Normal |
| C-65-5 | 33 | Negative | 45(XO) | 4.9 | 6.1 | | >96 m.u. | Normal |
| C-65-6 | 34 | Positive | 46(XX) | 7.0 | 6.0 | | >6 m.u. | Normal |
| C-65-24 | 23 | Positive | 46(CC) | 8.6 | 5.1 | | >16 m.u. | Normal |

* Normal values: 5–60 m.u.
5–10 R.U.

XO/XX/XXX (case report 5). A summary of these patients is shown in table 5.

**TABLE 5: Chromosome Analysis in Patients With Secondary Amenorrhea**

| Patient Code | Age Age at Menarche | Height | Sex Chromatin Body Per cent | Karyotype |
|---|---|---|---|---|
| C-65-44 | 26/12 | 5′3″ | 29 | 46(XX) |
| C-65-40 | 22/12 | 5′3″ | 29 | 46(XX) |
| C-65-31 | 19/14 | 5′3″ | 35 | 46(XX) |
| C-65-19 | 16/12 | 5′7″ | 60 | 46(XX) |
| C-65-16 | 22/14 | 5′6½″ | 45 | 46(XX) |
| C-65-10 | 16/9 | 4′9″ | 57 | 46(XX) |
| C-66-38 | 25/11 | 5′2½″ | 45 | 46(XX) |
| C-66-46 | 20/13 | 5′3½″ | 40 | 46(XX) |
| C-66-51 | 18/17 | 5′2″ | 19/26 | 46(XX) |
| C-66-57 | 19/13 | 5′3″ | 60 | 56(XX) |
| C-66-49 | 33/11 | 5′7″ | 20 | 45(XO)<br>46(XX)<br>47(XXX) |

Nine postpuberal patients had primary oligomenorrhea. Phenotypical characteristics were normal, and chromosomal analysis revealed a normal sex complement in all 9. Sex chromatin studies were distinctly positive in every case. A summary of the results is shown in table 6.

**TABLE 6: Cytogenetic Studies in Patients with Primary Oligomenorrhea**

| Patient Code | Age/ Age at Menarche | Height | Sex Chromatin Body | Karyotype |
|---|---|---|---|---|
| C-65-50 | 19/14 | 5′5″ | Positive | 46(XX) |
| C-65-49 | 17/14 | 4′8½″ | 40% | 46(XX) |
| C-65-47 | 23/13 | 5′1″ | 40% | 46(XX) |
| C-65-43 | 22/12 | 5′4″ | Positive | 46(XX) |
| C-65-32 | 20/17 | 5′2½″ | Positive | 46(XX) |
| C-66-34 | 30/12 | 5′2″ | Positive | 46(XX) |
| C-66-42 | 28/13 | 5′3½″ | Positive | 46(XX) |
| C-66-44 | 16/11 | 5′4″ | Positive | 46(XX) |
| C-66-54 | 16/11 | 5′2½″ | 40% | 46(XX) |

Table 7 summarizes the chromosomal analysis as related to menstrual variation in all patients studied.

**TABLE 7: Chromosomal Analysis as Related to Menstrual Variation**

| Menstrual Pattern | Total Cases | Karyotype Analysis | | Sex Chromatin | |
|---|---|---|---|---|---|
| | | Normal | Abnormal | Positive | Negative |
| Primary amenorrhea | 9 | 3 | 6 | 4* | 5 |
| Secondary amenorrhea | 11 | 10 | 1 | 11 | |
| Primary oligomenorrhea | 9 | 9 | | 9 | |

* One double positive.

### Illustrative Cases

**Case 1** (C-64-28). This infant, born at term to a 24-year-old primigravida, displayed multiple congenital malformations (figure 1) and died shortly after birth. Postmortem examination showed acute bilateral pneumonitis. Anomalies present were acrocephaly, hypotelorism, defect of posterior palate, persistence of Rathke's pouch, syndactylism, and extra digits. The external genitalia showed unfused scrotal sacs, solid phallus, and perineal urethra. Testes were found in the right inguinal canal and left peritoneal cavity and were connected by the spermatic cord to the left inguinal canal (figure 2). The various anomalies suggested embryopathy at the sixth and eighth gestational week.

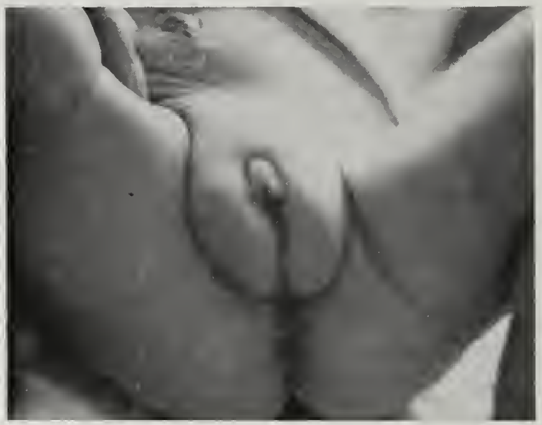

**FIG. 1. Case 1. Male pseudohermaphrodite with unfused scrotal sac, solid phallus, and perineal urethra.**

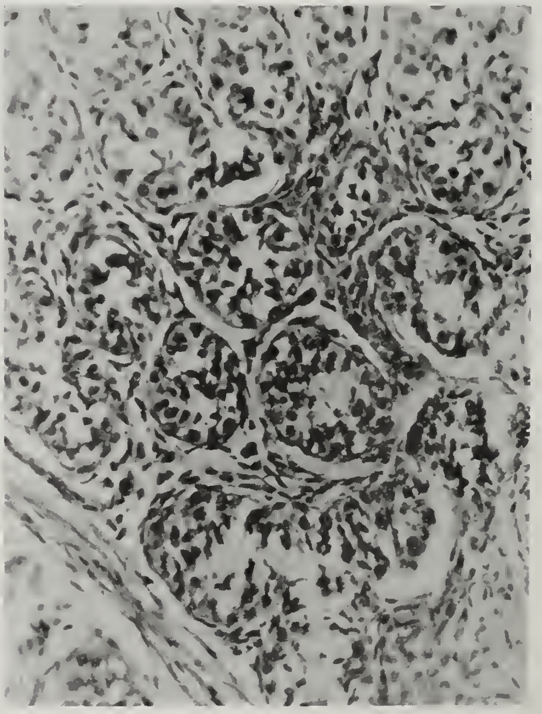

**FIG. 2. Case 1. Section of immature testis.**

The pregnancy history showed persistent glycosuria. The fasting blood sugar was normal, but the glucose tolerance test was borderline. Moderate hydramnios was noted.

Attempts to culture several tissues for chromosomal analysis failed. The diagnosis of a male pseudohermaphrodite was based upon the gonadal findings and a negative sex chromatin pattern in sections from different tissues (figure 3).

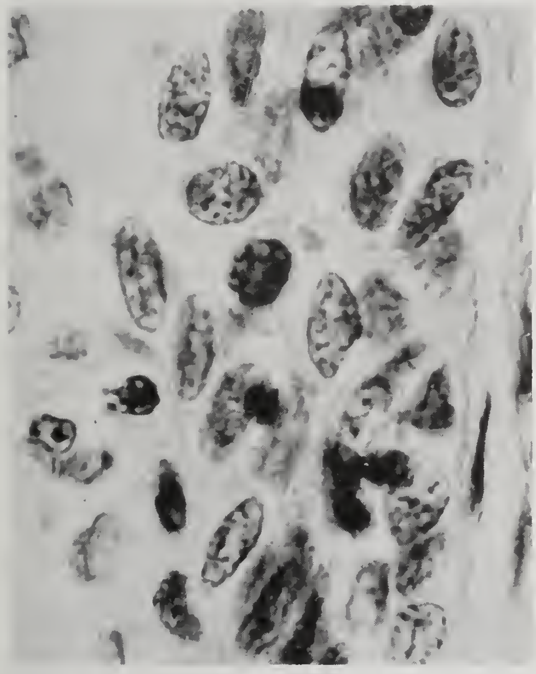

**FIG. 3. Case 1. Negative sex chromatin cell-pattern in tissue section.**

**Case 2** (P-64-150). This patient was born of a full-term pregnancy and uncomplicated delivery to a gravida III who had 2 previous abortions at 3 and 14 weeks. The birth weight was 5 lbs. 10 oz. There were multiple congenital anomalies. The infant developed sepsis and died at the age of 6 weeks.

Postmortem examination showed that bronchopneumonia was the immediate cause of death. The following anomalies were noted: micrognathia, cleft palate, microglossia, hypotonia, low-set ears, supernumerary digits on the hands and feet, calcaneovalgocavus, congenital absence of the twelfth ribs and coccyx, webbed neck, and simian lines of the palms. The external genitalia showed hypertrophy of the clitoris and large labia majora (figure 4). The internal genitalia consisted of a uterus, but fallopian tubes were not identified. Gonads were represented by a testis on the right side measuring 0.8 by 0.6 cm. Histologic examination showed well-formed tubules containing Sertoli cells and immature germ cells. Spermatogonia were present in the lumens of almost all of the tubules, and there was no evidence of Leydig cells. The structure of the left gonad was consistent with that of an ovotestis. The chromosomal analysis from peripheral blood culture showed the majority of cells to be 46(XO)-trisomy 21 (figure 5), but a minor cell line of 47(XY)-trisomy 21 was noted in the connective tissue culture.

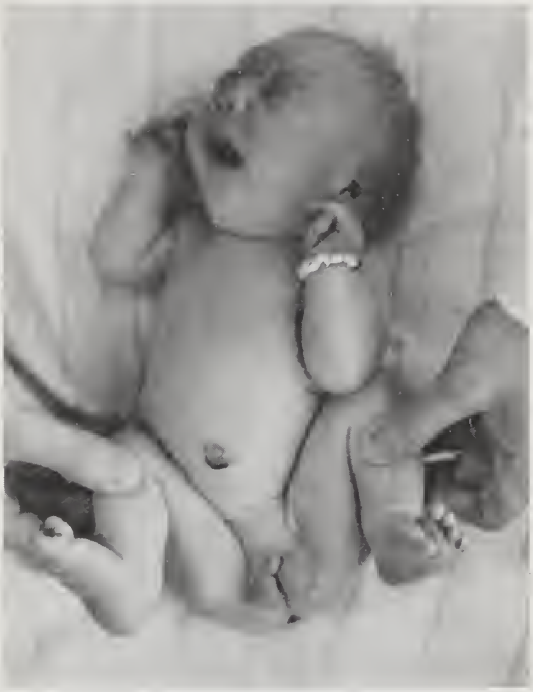

**FIG. 4. Case 2. True hermaphrodite with multiple congenital anomalies.**

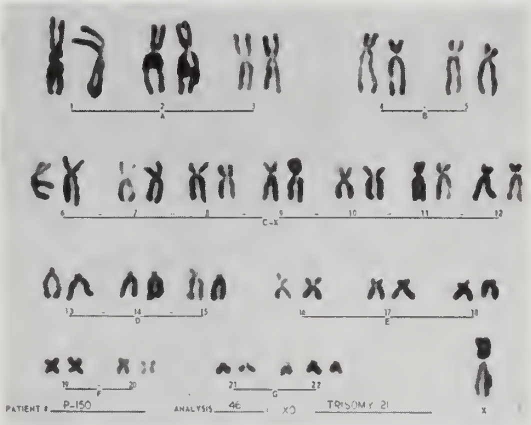

**FIG. 5. Case 2. Karyotype, showing predominant pattern of 2 cell lines present in blood culture (trisomy 21, XO).**

**Case 3** (H-66-681). This 27-year-old patient was seen by one of us (J. M.) at the Hospital San Ignacio in Bogota, Colombia because of primary amenorrhea The classical diagnostic features of the syndrome of testicular feminization were present. Normal breast development was present, but pubic and axillary hair had not developed (figure 6). Laparotomy revealed the absence of müllerian development and the presence of right and left gonads (figure 7—A and B), which on

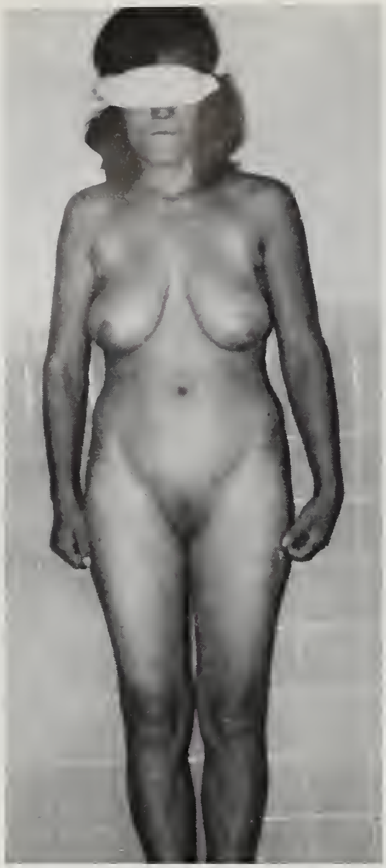

FIG. 6. Case 3. Patient with testicular feminization syndrome.

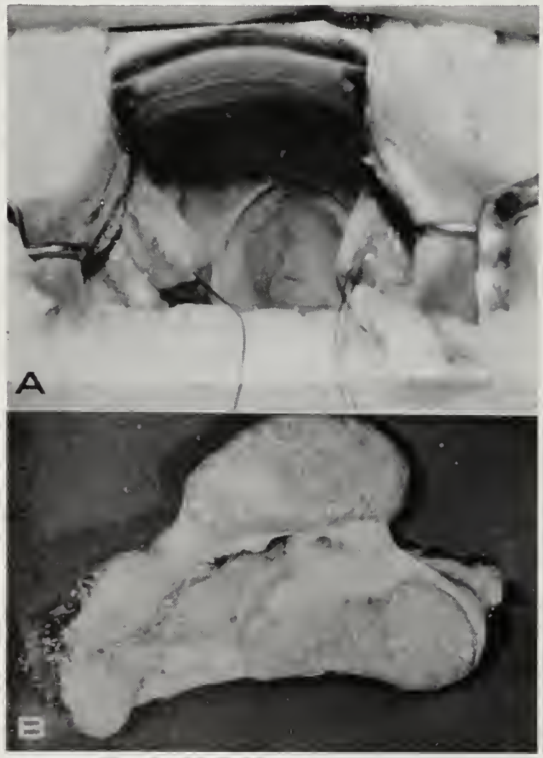

FIG. 7. Case 3. A. Laparotomy, showing location of testes (note threads attached). B. Left testis sectioned into 2 fragments.

histologic examination showed as immature testes (figure 8). Sex chromatin on buccal smears was negative, and chromosomal analysis revealed a 46(XY) chromosome pattern.

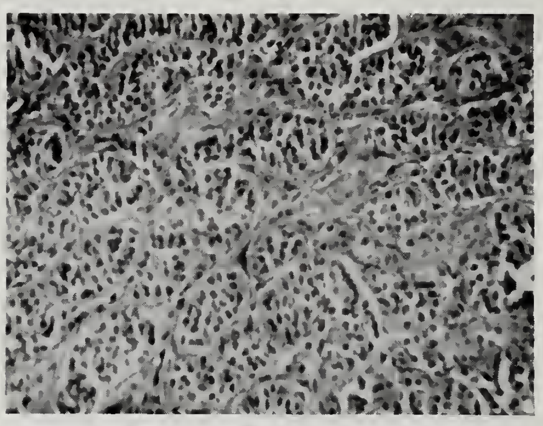

FIG. 8. Case 3. Section of immature testis.

**Case 4** (C-64-46). A 21-year-old white woman was referred to our laboratory with a diagnosis of primary amenorrhea. She reported a single sibling, a sister (aged 26) who began her menses at 12 and is currently married, with a normal child. Their mother (aged 61) had a normal menarche and menses until menopause at the age of 50. The patient was 4 feet, 11 inches tall and weighed 145 lbs. She had scant pubic and axillary hair, low hair line, poor breast development, and cubitus valgus but no appreciable webbing of the neck (figure 9). Pelvic examination under anesthesia showed in-

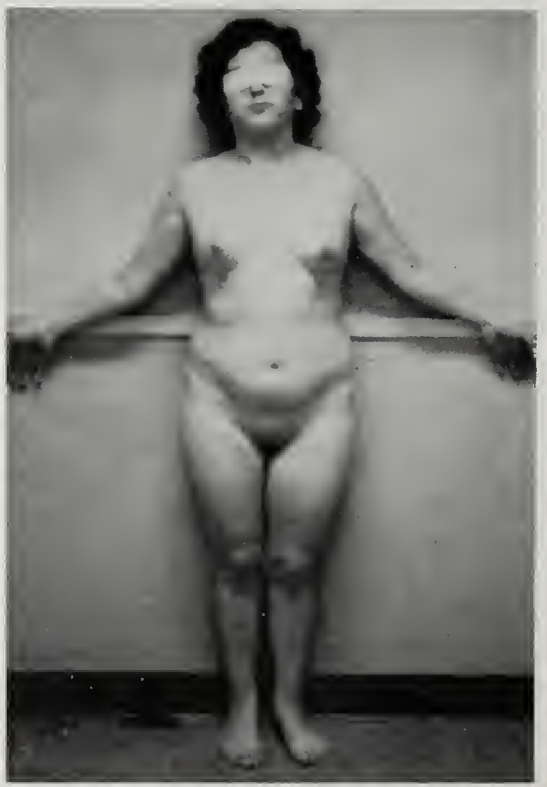

FIG. 9. Case 4. Patient with Turner's syndrome. Note absence of webbing of neck.

fantile external genitalia, an adequate vagina, and a small cervix, but a uterine body was not palpable.

Protein-bound iodine was 4.7 mcg., $T_3$ uptake was 92 per cent, 17-ketosteroids were 16.2 mg./24 hr. with similar levels on repeated determinations. The follicle-stimulating was 9 R.U. A first determination of urinary estrogens was 127 mcg./24 hr. and a second, 91 mcg./24 hr. X-ray films of the skull were normal.

Sex chromatin of a buccal smear was reported as 6 per cent positive. Chromosomal analysis in peripheral blood culture cells showed a modal of 45(XO). The possibility of XO/XX mosaicism is to be explored by subsequent skin biopsy.

**Case 5** (C-66-49). This patient is a white woman referred for cytogenetic studies at the age of 33. Menarche occurred at 12 years followed by increasingly irregular menses, until the age of 28 when she experienced periods of amenorrhea lasting as long as 5 months. At that time she was placed on oral contraceptive medication in order to regulate her menses. The referring gynecologist advised her to discontinue this medication in order to have endocrine studies made. She has been amenorrheic since.

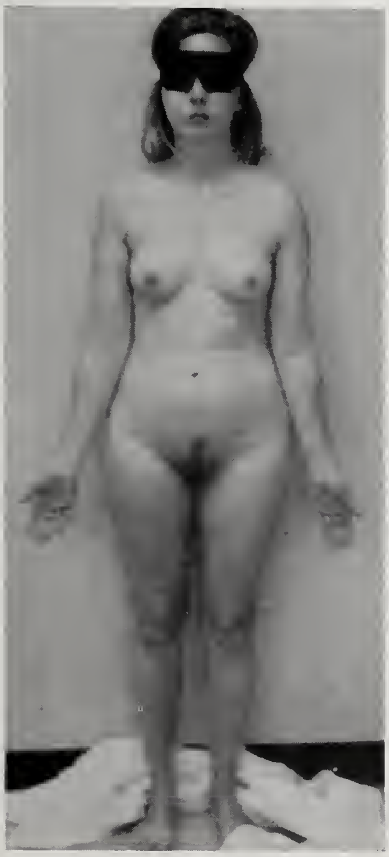

FIG. 10. Case 5. Normal phenotypic appearance.

There was normal development of the secondary sex characteristics (figure 10). The height was 5 feet, 7 inches. The external genitalia were normally developed, the uterus was of small size, and the ovaries could not be palpated. Hormonal evaluation on vaginal cytology showed a low estrogen effect. The first gonadotrophin determination was very low and considered unsatisfactory. A repeat determination was reported as less than 6.6 m.u./24 hr. Visual fields and X-ray films of the sella turcica were normal. The sex chromatin on buccal smear showed 20 per cent positive; double Barr bodies were observed (figure 11—A and B). Chromosomal analysis of peripheral blood culture showed the following mosaic pattern: 46(XX) 85 per cent, 45(XO) 10 per cent, and 47(XXX) 5 per cent (figure 12—A, B, C). A diagram of the mechanism of production of this mosaic is shown in figure 13.

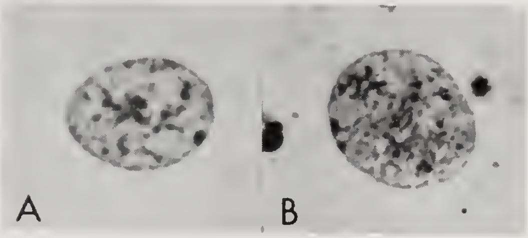

FIG. 11. Case 5. A and B. Sex chromatin as single and double Barr bodies in same buccal smear specimen.

**Case 6** (C-666). This 17-year-old Negress was ascertained in a cytogenetic survey at an institution for the mentally retarded to show a double sex chromatin pattern. The patient is 5 feet, 10 inches tall and weighs 128 pounds. The phenotype is grossly that of a female and the breast development is moderate. The somatotype is consistent with a gynandromorphic, since the shoulders and pelvic girdle appear masculine (figure 14). Secondary sexual development, other than some periareolar fullness, is absent. At the time the photograph was taken the patient was amenorrheic, but the menses were spontaneously initiated at the age of 18½. Secondary sex development, other than moderate pubic and axillary hair, has not been pronounced. Repeated chromosomal analysis from peripheral blood cultures consistently showed a 47(XXX) pattern.

## Discussion

At present the underlying mechanisms which determine human phenotype along male or female lines are only partially understood. Embryonic development of internal and external genitalia usually follows an orderly pattern in which the genetic constitution of the individual, the inductive capacity of the formed genitalia, and gonadal or extragonadal hormonal influences all play major sequential roles. Humans exhibit a double potential of sexual differentiation. Sex dimorphism is the end-result of the suppression or lack of suppression of müllerian development which is determined at the time of conception. Castration experiments in different mammals have shown that the female is the neuter line of development, and that removal of the gonads at an early developmental stage will unequivocally produce a phenotypic female.[5, 6, 7]

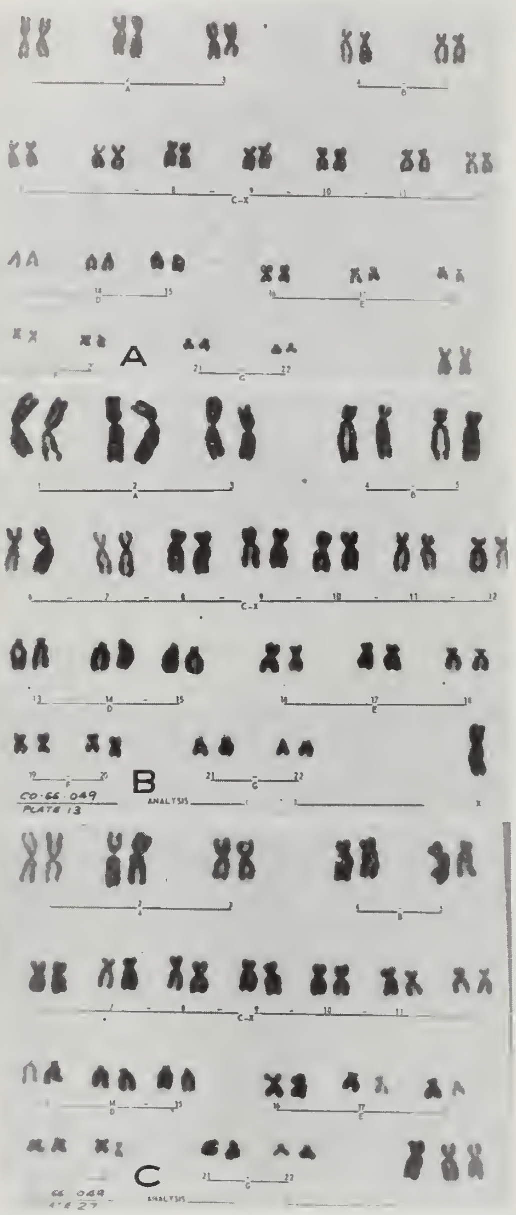

**FIG. 12. Case 5. A, B and C. Karyotypes showing the 3 cell lines—XX (normal), XO, and XXX.**

The role of the testes as an active suppressor of müllerian duct development is generally accepted, but in the case of true hermaphrodites the ovotestis appears to behave as an ovary.[8, 9] The early gonad is bipotential, and development of testes and ovary in the initial embryogenic stages follows the same pathways regardless of the genetic sex. The precise role of germ cells in gonadal differentiation is not clear. Although germ-cell absence does not prevent initiation of gonadal development, final and complete gonadal differentiation depends upon the presence of sufficient numbers of germ cells.[10]

The major masculinizing influence is based upon the presence of the Y chromosome, since testes have not been observed to develop in its absence. One exception is true hermaphroditism with an XX sex complement,[9] but exclusion of mosaicism incorporating a Y chromosome in one of the cell lines is difficult to rule out. Cases with ovotestis and an XO/XY mosaic pattern have been reported.[11, 12, 13] Differentiation of the urogenital sinus is also under gonadal influence, and the effect of an ovotestis at this site appears to be male-differentiating but with a weak biologic influence.[9]

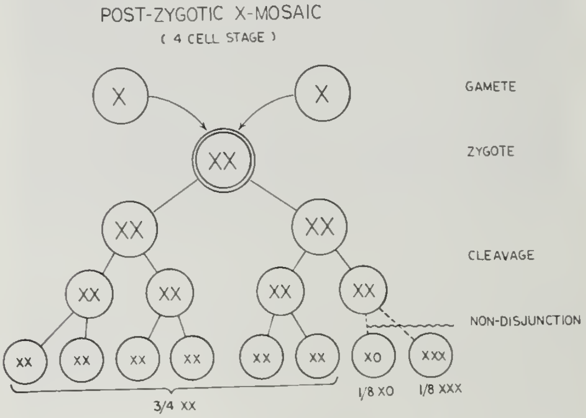

**FIG. 13. Case 5. Diagram showing suggested mechanism of production of X mosaic.**

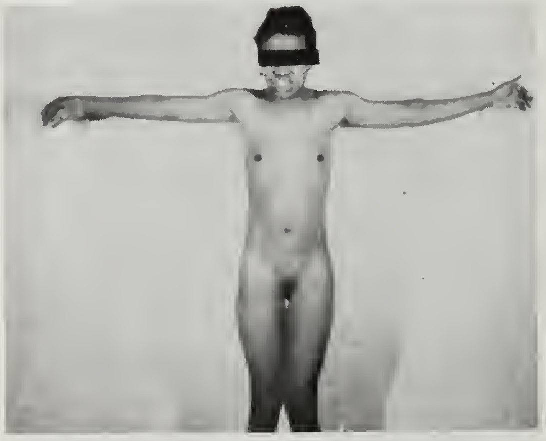

**FIG. 14. Case 6. Triple-X female.**

The exogenous hormonal and other environmental alterations of external genital development and secondary sex characteristics have been actively discussed in the literature.[14-20] However, the basic question in sex differentiation remains unsolved, i.e., the biochemical mechanisms by which sex-determining genes act upon the genital primordia. A diagram outlining the various realms of sexual differentiation and identification confronting the clinician is given in figure 15.

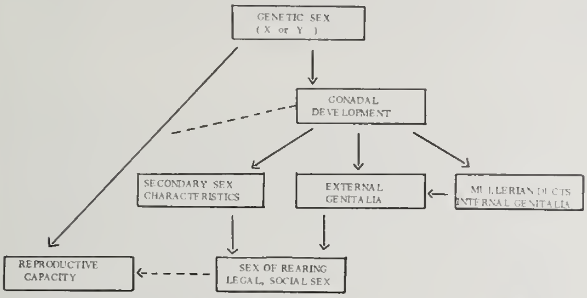
GENETIC SEX
( X or Y )
GONADAL DEVELOPMENT
SECONDARY SEX CHARACTERISTICS
EXTERNAL GENITALIA
MULLERIAN DUCTS INTERNAL GENITALIA
REPRODUCTIVE CAPACITY
SEX OF REARING LEGAL, SOCIAL SEX

**FIG. 15. Diagram showing sequence of sexual differentiation and identification.**

The diversity of anatomic, endocrine, and cytogenetic features encountered in sexual developmental anomalies accounts for the lack of a satisfactory classification. Androgenic substances administered during pregnancy are known to induce female pseudohermaphroditism in the human.[14, 15] It has been noted, however, that synthetic androgens differ from fetal testicular products in that they do not inhibit development of the müllerian duct system in mammals.[16] In the cases of female pseudohermaphroditism observed by us the search for a possible iatrogenic source of masculinizing hormonal influence was unproductive. Nor was the most common form of detectable aberrant sexual development which is associated with the congenital virilizing adrenal hyperplasia syndrome observed by this study group.

Estrogens administered during pregnancy have been reported to produce both male[17] and female[18] pseudohermaphroditism, but pregnancy histories in our patients were negative in this respect. Male pseudohermaphroditism includes a spectrum of anatomic variations ranging from mild hypospadias to fully developed müllerian derivatives. A loss of inductive control of fetal testis over the accessory sex organs has been suggested in the pathogenesis of this anomaly, but the nature of the masculinizing factors is still obscure.[16]

In case 1 (code C-6428), in addition to maldeveloped external genitalia other congenital malformations were present which permit us to speculate that they might have been the result of a common causation between the sixth and eighth weeks of embryonic development.

The patient in case 2 (code P-64150) also displayed several congenital malformations which may be chronologically related. In this patient, however, 2 types of nondisjunction phenomena must have occurred. The first, a meiotic nondisjunction giving origin to trisomy 21–22, subsequently followed by a postzygotic error in mitosis which produced XO and XY cell lines, is hypothesized. The influence of the XY line in early embryogenesis was sufficient to cause the gonad to differentiate toward the testicular line, but müllerian duct development followed that of an immature female, since the internal genitalia were consistent with that of a female. In this case masculinization of the external genitalia may reflect some active androgenic response from the testes as inferred by the histologic features of the right gonad.

The significance of clitoral hypertrophy in X-monosomy has been the subject of previous consideration in the literature.[21] An excellent example of the continuum between the classical Turner syndrome (XO) and a more advanced male intersexuality presumably stemming from an XO/XY mosaicism has been recently reported by Russell et al.[11]

Case 3 (code H-66-681) illustrates the feminizing type of male pseudohermaphrodite designated as testicular feminization syndrome.[22] These phenotypic females usually have an XY sex chromosome complement, although 2 exceptions have been reported in which mosaicism was present (XO/XY/XX[23] and XY/XYY/XXY[24]). At puberty breast development occurs normally in these patients (figure 6), but sexual hair is scant or absent and does not respond to the exogenous administration of androgens.[25] Müllerian development is absent or very rudimentary. External genitalia are infantile and the vagina is represented by a blind pouch. The gonads are immature testes located anywhere in the path of the round ligaments. The absence of the masculinizing effect in the presence of normal adult male plasma levels of testosterone[26-29] and production rates of plasma testosterone[30] support the theory earlier suggested by Wilkins[25] of a refractoriness to the male hormones. The familial incidence of this syndrome indicates that it is genetically determined. As judged from pedigree analysis, the mode of inheritance is that of a male-limited autosomal dominant.[31, 32, 33]

Of great concern in infants with ambiguous external genitalia are the exclusion of congenital virilizing adrenal hyperplasia in the newborn period, particularly because of its immediate medical implications, and the assignment of sex for rearing. Cytogenetic analysis is certainly helpful in both respects. Assignment of rearing sex should be made on the basis of the anatomic configuration of the external genitalia and the morphology of the gonad. In certain instances, however, as it occurs in some hermaphrodites[8] and in patients with testicular feminization syndrome, the assignment of rearing sex may have to be contrary to the sex chromosomal constitution.

Case 4 (code C-6446) is an example of Turner's syndrome in which webbing of the neck was not present (figure 9). Phenotypical variations of the classical Turner description[34] are not infrequently observed. It has been suggested that X-monosomy would be a more adequate term to designate this type of chromosomal aberration, since recognition of this genetic entity is possible in the newborn.[35] In addition, a familial occurrence of the somatic characteristics of the syndrome with an apparently normal sex chromosomal complement has recently been reported in 2 sibships.[36]

The patient in case 5 (code C-6649) revealed XO/XX/XXX mosaicism. Since the phenotypical characteristics of this patient are well within normal limits (figure 10), the more serious implications of her genetic defect are those of her fertility potential. In this regard the chromosomal constitution of the gonads is most important. We believe, however, that gonadal biopsy is indicated only if a laparotomy has to be performed for some other indication or if the patient contemplates marriage.

Case 6 (code C-666) represents another type of X-aneuploidy, that of the triple-X female, first described by Jacobs as superfemale.[37] These patients usually have menses and are able to reproduce. Failure to observe chromosomal abnormalities in their progeny[38] may indicate a preferential segregation by which the XX containing secondary oöcyte becomes the polar body and the X-containing oöcyte gives rise to the ovum.[23]

Most of these patients, as in our case, have been detected by screening patients in mental institutions, thus giving the increased association with mental retardation. This higher incidence may only represent a bias of ascertainment.

## Summary

Over a 2-year period 36 patients were selected for study at the Columbia Hospital Cytogenetic Research Laboratory on the basis of ambiguity of the external genitalia in the prepuberal group and various patterns of menstrual failure in the postpuberal group. The clinical aspects and the cytogenetic findings of 6 patients with different sexual developmental anomalies have been presented in case reports and discussed.

The group yielding the greatest number of chromosomal aberrations was that having primary amenorrhea; of these, X-monosomy was the most frequent abnormality. A case of XO/XX/XXX mosaicism was detected in a phenotypically normal female with secondary amenorrhea. No cytogenetic abnormalities were found in patients with oligomenorrhea.

Sex chromatin studies and chromosome analysis were found to be extremely useful in elucidating the etiology of many sexual abnormalities. Negative findings in cytogenetic evaluation were viewed with caution, since the presence of mosaic patterns is difficult to rule out without further diagnostic procedures.

Over half of the patients with primary amenorrhea were over the age of 30 at the time of referral. Study of these patients at an earlier age would have favored the possibilities of therapy in order to modify some of the abnormal phenotypical characteristics.

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*(Continued on page 470)*

# Placental Polyp as a Cause of Late Puerperal Hemorrhage

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THE PLACENTAL POLYP is a poorly recognized cause of late puerperal hemorrhage. Since Hagstrom[1] reported the initial case of placental polyp in 1940 only 14 cases have been reported in the American literature,[2-9] but this condition occurs far more frequently than has been reported. It complicates term pregnancy in most instances in which it occurs.

We have reviewed the medical records of the Columbia Hospital for Women for the 3-year period, July 1, 1963 through June 30, 1966. There were 14,775 deliveries during this time. Six patients with placental polyps, confirmed by tissue examination, were uncovered. The case history summaries are presented to illustrate the pertinent clinical and pathologic aspects of this condition.

## Report of Cases

**Case 1.** H. S. (S-63-1221), a 41-year-old white woman, gravida II, Para 1, previous miscarriage 1, was admitted to the Hospital because of menometrorrhagia of 5 months' duration. She had missed her menstrual period 1 month. The following months she experienced frequent intermittent vaginal spotting and prolonged menstrual flow. The uterus was irregularly enlarged to 10–12 weeks' gestational size with palpable bilateral adnexal enlargement. A preoperative diagnosis of uterine fibroids was made. At operation multiple intramural and subserous leiomyomata of the uterus with bilateral "chocolate cysts" of the ovaries were found. Total abdominal hysterectomy and bilateral salpingo-oöphorectomy were performed. On opening the uterus an elongated, reddish, polypoid lesion (1.8 by 1 by 1 cm. in size) was discovered attached to the fundal area of the uterine cavity. The base of the polyp was firm, while the apex was soft, friable, and hemorrhagic. The microscopic examination of the polyp showed a central core of preserved and poorly preserved chorionic villi which were surrounded by degenerating decidua and deposits of fibrin. At the base of the polyp there was an irregular thin rim of decidua incompletely separating the chorionic villi from the myometrium. The leiomyomata were typical in appearance. Both ovaries showed evidence of endometriosis.

**Case 2.** E. V. (S-63-2634), a 31-year-old Negress, gravida I, Para 1, presented herself with the chief complaint of menometrorrhagia of 2 months' duration. Pelvic examination revealed an irregularly enlarged, firm uterus, estimated at 16 weeks' gestational size. A preoperative diagnosis of uterine fibroids was made. Total hysterectomy was performed. The uterus contained multiple leiomyomata. The uterine cavity was lined by a yellowish-tan endometrium. There was a small reddish, polypoid lesion located high in the endocervical canal at the endometrial junction. Microscopic examination of this polypoid lesion showed a partially necrotic, hemorrhagic, and inflamed mass within which trophoblastic villi and decidual cells could be recognized. The base of the polyp was formed by the blood vessels and a thin layer of decidual cells. The blood vessels in this area were ectatic and enlarged, and had thickened hyalinized walls. The multiple leiomyomata were typical in appearance.

**Case 3.** A. S. (S-64-2314), a 22-year-old Negress, gravida II, Para 2, was admitted to the Hospital with vaginal bleeding accompanied by lower abdominal cramps of 2 weeks' duration. The vaginal bleeding had been preceded by 6 weeks of amenorrhea. The uterus was slightly enlarged. The immunologic pregnancy test was negative. A tentative diagnosis of missed, incomplete abortion was made. Six grams of grayish-pink to pinkish-red, hemorrhagic uterine contents were obtained by curettage of the uterine cavity. Some of these fragments had a polypoid appearance. The largest polypoid mass measured 1.4 cm. by 1 by .8 cm. Microscopic examination of the nodular mass showed decidual tissue with extensive necrosis, acute inflammation and hemorrhage. In one area viable-appearing chorionic villi were present within this mass of decidual cells. Other fragments showed degenerating villi which were embedded in deposits of fibrin and red blood cells. Fragments of nonsecretory endometrium were also present and exhibited focal changes of severe chronic endometritis.

**Case 4.** R. E. (S-64-4275), a 28-year-old, gravida II, Para 3, white woman, who was at the twenty-third postpartum day, was admitted to the Hospital with sudden onset of severe vaginal bleeding. The last pregnancy had been terminated at 29 weeks of gestation with spontaneous labor and the delivery of premature twin infants. The fourth stage of labor was completed by manual removal of the retained placenta.

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The uterus was enlarged and boggy. The cervix was relatively clean and patent. The preoperative diagnosis was subinvolution of the uterus with retained secundine. No dilation of the cervix was necessary. The uterine cavity was sounded to a depth of 4.5 inches. Curettage of the uterus was performed. A small amount of reddish, flaccid blood clots was obtained. In addition, there were multiple firm, nodular fragments of yellowish tan tissue.

Microscopic examination revealed a polypoid nodule which was composed of necrotic chorionic villi. There were small ectatic pools of blood in what appeared to be intervillous sinuses. The outer rim of the nodule showed an acute inflammatory cellular reaction of numerous neutrophils and fibrin. The base of the polyp contained thick-walled, ectatic blood vessels.

**Case 5.** M. H.(S-65-2314), a 40-year-old white woman, gravida II, Para 2, was admitted to the Hospital with the chief complaint of menometrorrhagia in the last 2 months after having had 1 missed period. The latest menstrual period occurred a week early and lasted for 7 days up to the day of admission. It was characterized by moderate dark to bright red spotting. The patient had had a uterine myomectomy and ovarian chocolate cyst removed 12 years previously. The uterus was normal in size, and a small polyp was seen in the cervical canal. The base of the polyp could not be seen. The preoperative diagnosis was cervical polyp with menorrhagia, cause undetermined. Dilation and curettage with cervical polypectomy were planned. The polyp was exposed and removed by torsion with an ovum forceps from a location high in the endocervical canal. The cervix was then dilated and the cavity of the uterus curetted. The polyp consisted of a relatively firm, nodular mass of deep reddish-blue tissue. It measured 1.5 by 0.8 by 0.3 cm.

Microscopic examination of the polyp revealed an arrangement of chorionic villi and decidual cells, covered by fibrin and enclosing a central core of thick-walled blood vessels. The chorionic villi were degenerated and necrotic in appearance. The vessels were surrounded by neutrophils, lymphocytes, and monocytes. The uterine curettings showed secretory-type endometrium. In addition, there were several small fragments containing hyalinized blood vessels and what appeared to be degenerating decidua.

**Case 6.** F. S. (S-65-2317), a 23-year-old, gravida O, white woman, stated that her menstrual periods had been irregular since the menarche at age 12. She was admitted to the Hospital because of menometrorrhagia of 2 months' duration prior to admission. The PBI was within normal range. The cytologic smear was negative. Pelvic examination revealed essentially normal external genitalia. The cervix was firm and clean. The uterus was normal in size and shape. The adnexa were negative. Dilation and curettage was performed with the preoperative diagnosis of menometrorrhagia, etiology undetermined. A single fragment of polypoid tissue was obtained from the posterior wall of the uterine cavity. It measured 1 by 0.5 by 0.3 cm. in size and was mottled in color, ranging from yellowish to reddish-brown. The remainder of the uterine curettings were not remarkable and were sparse in amount.

On microscopic study this polypoid nodule displayed an exterior rim of acutely inflamed and necrotic fibrinous tissue. The central core of the nodule was composed of degenerating hyalinized chorionic villi. These were infiltrated by acute inflammatory cells. The remaining curettings were composed of small fragments of endometrium whose glands showed a mild atypical hyperplasia with evidence of chronic endometritis.

## Discussion

The diagnosis of placental polyp is not commonly made preoperatively. It seldom is even considered. The signs and symptoms are not particularly characteristic. Placental polyp occurs most frequently in the postpartum period, but it may follow a recent abortion. The patient complains of intermittent vaginal bleeding and occasionally of crampy abdominal pains. The onset of bleeding is sudden and may persist 2 to 3 weeks until the polyp is removed. The severity of the hemorrhage varies considerably but may be life-threatening at times. Pelvic examination frequently reveals an enlarged, boggy uterus.

The placental polyp is a localized, polypoid mass of retained placental tissue. It varies considerably in size and location of attachment. The retained tissue may be the end-result of an accessory lobe or a part of the placenta. It exists in a more or less viable state. Recognizable decidua vera incompletely surrounds the vascularized base of the polyp at its uterine attachment. There is no deep penetration of the myometrium. The chorionic villi contained in the polypoid mass exhibit all degrees of viability. These villi are enmeshed in fibrin deposits which are infiltrated by numerous neutrophils. The uterine bleeding is invoked by the inflammatory process which smoulders about the ectatic blood vessels at the base of the placental polyp. Any irregularity in association with periods therefore makes this bleeding indistinguishable from menometrorrhagia.

The 6 case histories presented in this paper illustrate the wide range of clinical situations that confront the gynecologist. The patients of cases 1 and 2 both had menometrorrhagia which was presumed to be secondary to a fibroid uterus.

Since no history of abortion was elicited, the diagnosis of placental polyp was never included in the differential diagnoses. Hysterectomies were subsequently performed. A typical placental polyp was found in the uterine cavity in case 1 and another polyp was discovered in the internal os area in case 2. It is uncertain how long either of these polyps was present since there was no history of previous abortion or pregnancy. The patient of case 3 was thought to have an incomplete abortion in view of her recent menstrual history. The tissue recovered from a diagnostic dilation and curettage showed evidence of endometritis and placental polyp. Case 5 illustrates another polypoid mass arising high in the cervical canal close to the internal os. The history was suggestive of a miscarriage. The patient had missed a single period prior to the onset of the vaginal bleeding. The patient of case 6 exhibited dysfunctional bleeding. There was no note implicating a previous pregnancy. Again, diagnostic dilation and curettage produced evidence of chronic endometritis with reactive endometrial hyperplasia and a placental polyp. Case 4 was the only one of the 6 in which the history was almost pathognomonic of a placental polyp. There had been a recent delivery of twins and a manual removal of the placenta.

In 2 of 3 cases of placental polyp reported by Kurtz and Comando[6] the third stage of labor was forcibly shortened by manual removal of the placenta before the normal third stage uterine activity commenced. With such a maneuver a small fragment of placenta may be retained. This then acts as the nidus for the development of a placental polyp. Wolfe and Pedowitz[8] reported 2 cases of placental polyp occurring in 32 patients who had a clinical diagnosis of retained placental fragments. Spontaneous expulsion of retained placental fragments normally can be expected before the tissue undergoes organization and attaches itself to the uterus. Huffman[10] stated that a fragment of placenta which remains attached to the uterus may undergo partial necrosis with deposition of fibrin upon its surface and thus take on the form of a placental polyp. Reid[11] claims that the placental polyp is related in some fashion to a previously unrecognized focal type of placenta accreta. Hoberman et al supported this view. We also find evidence in support of this statement. It has been shown that the placental polyp may remain within the uterine cavity indefinitely. This is well documented by Baldwin,[5] Hoberman et al,[9] and Greenhill.[7] All of these authors described patients in whom a placental polyp had been found for periods of time up to 4 or 5 years within the uterine cavity before clinical symptoms occurred.

Late postpartum bleeding should raise the possibilities of subinvolution of the placental site, postpartum endometritis, retained secundine, and choriocarcinoma. Other diagnoses which may be considered are those of primary uterine malignant lesion, endometrial polyp, endometrial hyperplasia, submucous fibroid, withdrawal hormonal bleeding, and unrecognized trauma. Therefore, careful consideration of all aspects of the patient's history and physical examination should be made.

In order to minimize or prevent the occurrence of placental polyp it would seem that conservative management of the third stage of labor is required. Thorough inspection of the placenta and exploration of the uterine cavity must be performed whenever the placenta is removed manually. The specific therapy consists of thorough curettage of the uterine cavity. In a very few cases hysterectomy may be resorted to in order to control the hemorrhage.

## Summary

The placental polyp is an uncommon cause of late postpartum bleeding. It is a sequela of localized retained placental fragment which has undergone organization and fibrin deposition forming a polypoid mass of varying size. It may be attached anywhere within the uterine cavity or endocervical canal. It usually has an associated defect in the decidua vera so that a localized placenta accreta situation is present. The placental polyp may remain in the uterine cavity indefinitely before it becomes clinically manifest. The severity of delayed puerperal hemorrhage varies from spotting to the point of threatening the patient's life.

There were 6 unsuspected cases of placental polyp reported over a 3-year period, during which time 14,775 term deliveries occurred.

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# Early Repair of Vault Vesicovaginal Fistula

JOSEPH B. SHEFFERY, M.D., F.A.C.S.*

In 1949 Ragan[1] reported that cortisone inhibited the formation of granulation tissue and fibroplasia and increased the growth of tissue macrophages. This stimulated Drs. Conrad Collins and Frederick Jones to employ this hormone in the treatment of severe pelvic infection in conjunction with antibiotic therapy "to prevent any cortisone spread effect."

They achieved excellent results and the once frozen pelvic organs regained partial to total mobility. Symptoms of pain and/or fever subsided completely in some, and in those cases in which symptoms persisted surgery was accomplished with little difficulty. In 1957 it occurred to them that the tissue surrounding rectovaginal and vesicovaginal fistulas was not unlike that observed in ligneous cellulitis of the pelvis, differing only in extent. It is common practice, even today, not to attempt to close these fistulas until 6 to 8 months after their occurrence, which is the length of time needed for the inflammatory exudate to subside.

They reasoned that if cortisone produced such desirable results in the therapy of pelvic cellulitis, and if the exudate surrounding vaginal fistulas was like pelvic cellulitis, the administration of cortisone might permit earlier surgical repair. Accordingly, they adopted the following routine: As soon as the fistulas were discovered postoperatively the patient was placed on 100 mg. of cortisone 3 times a day and given penicillin and a broad-spectrum antibiotic, all orally. A retention catheter was placed in the bladder during this time, and after 14 days of such therapy, if the fistula had not healed spontaneously, surgical correction was undertaken.

They noted no spread of infection and, conversely, observed that induration subsided in all cases and that the tissue after the 14 days of treatment had returned to near normal, allowing easy dissection and, most important, the accurate placing of sutures in tissue that did not tear. In 9 cases of vesicovaginal fistula they cured 8, with 1 failure.[2] In a personal communication with Dr. Conrad Collins I learned that he is still using this same routine and has continued to have excellent results.

At Columbia Hospital for Women we have had 3 cases of vesicovaginal fistula occurring at the vault of the vagina following abdominal hysterectomy. These fistulas all occurred during the first 10 postoperative days. The diagnosis of vesicovaginal fistula was made by placing cotton or gauze in the vagina, then emptying the bladder by catheterization and instilling through the same catheter a dilute sterile solution of methylene blue. Shortly thereafter the gauze or cotton is removed from the vagina and, if a fistula is present, it will be stained by the dye, and frequently the site will be visible at the vault.

Intravenous pyelograms and cystoscopic examinations were then performed and, when the final diagnosis of postoperative vesicovaginal fistula of the vaginal vault was made, the patient was placed on 100 mg. of cortisone 3 times a day, 500 mg. of Mysteclin-F® every 6 hours, and 400,000 units of oral penicillin 4 times a day—all orally. A Foley catheter was left in the bladder.

It was thought that, if immediate reapir could be done successfully while the patient was still in the hospital, the patient and the doctor would both be better satisfied and much happier. If the operative repair failed, the patient would be no worse off, since she would have had to wait 6 to 8 months for a repair if this technique had not been used. These patients were all operated on after being on cortisone, broad-spectrum antibiotics, and penicillin for 14 days by the following method:

The patient was anesthetized and placed in the lithotomy position. In 2 of the 3 cases it was necessary to do a left mediolateral Schuchardt type of incision to obtain good exposure of the vault, which is essential. The bleeding points in the mediolateral incision were ligated and retractors placed in the vagina. The bladder was catheterized, emptied, and then 100 c.c. of sterile milk solution (obtained from the Nursery) instilled into the bladder. The leaking area in the vault can then be easily identified (without staining the surrounding tissues as a methylene blue solution would). A Foley catheter was then fed into the fistula and inflated. For a very small fistula, in-

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fant-sized Foley catheters are available. The inflated catheter was then used for traction to bring the fistula down. If needed, lateral silk sutures can be placed at 10, 2, 4 and 8 o'clock to also help bring the fistula down (figures 1 and 2).

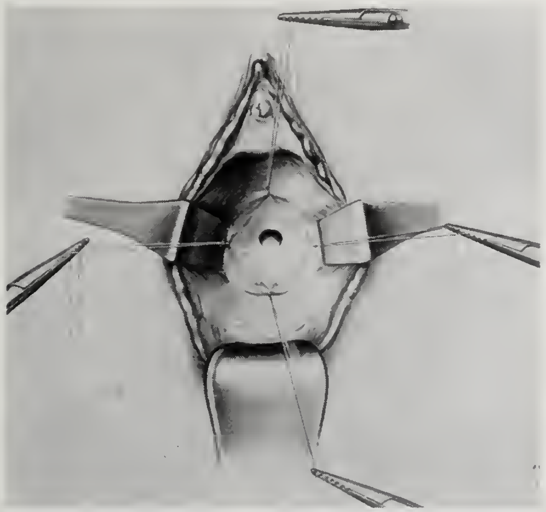

**FIG. 1. Four silk sutures are inserted so as to make the vault of the vagina accessible.**

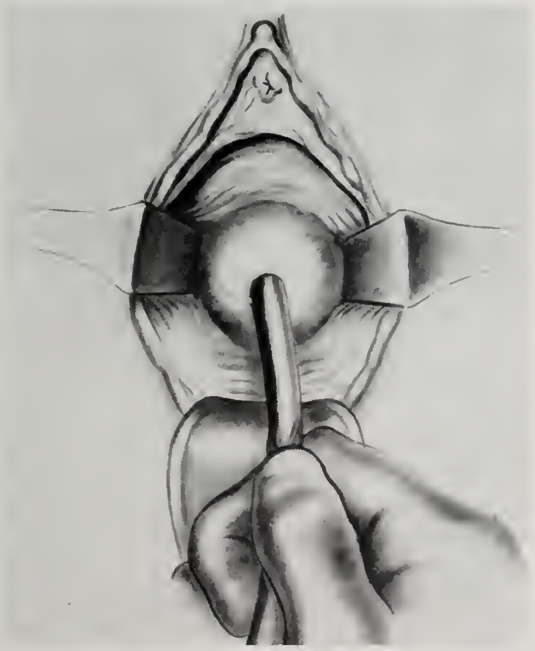

**FIG. 2. Foley catheter may be inserted for traction in exposing the area to be denuded.**

A square area at least 1.5 cm. from the center of the fistula was then outlined and divided into 4 quadrants with the back of the scalpel. The square area was dissected out, 1 quadrant at a time, starting with the right lower quadrant. No attempt was made to excise the fistula tract. After the right lower quadrant had been excised and bleeding controlled the left lower quadrant was excised, then the upper quadrants removed (figures 3 and 4).

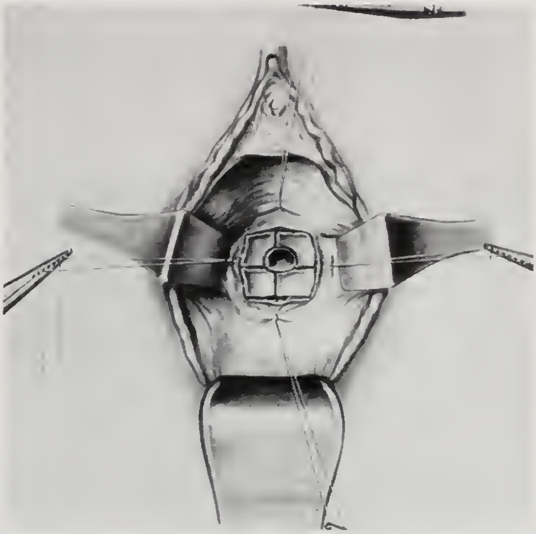

**FIG. 3. Four quadrants of vaginal mucosa are outlined for denudation. The fistulous tract is not denuded.**

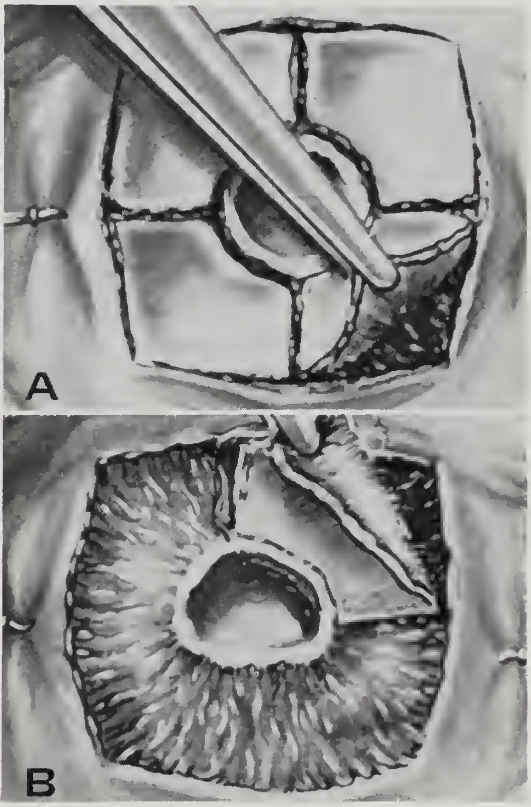

**FIG. 4. A. The quadrants are removed separately by sharp dissection with scissors. B. Note that the upper quadrants are removed last.**

When the tissue had been dissected free and all bleeding controlled, the first row of interrupted no. 00 chromic catgut sutures on an atraumatic needle was put in place (figure 5-A). The sutures were not tied, but hemostats were placed on each free end of the sutures. These hemostats are best placed on a ring forcep as each hemostat is applied, so that when all the sutures are in place one can easily identify the correct ends of sutures that are to be tied; otherwise they become twisted and much time is wasted in trying to find the correct ends to tie.

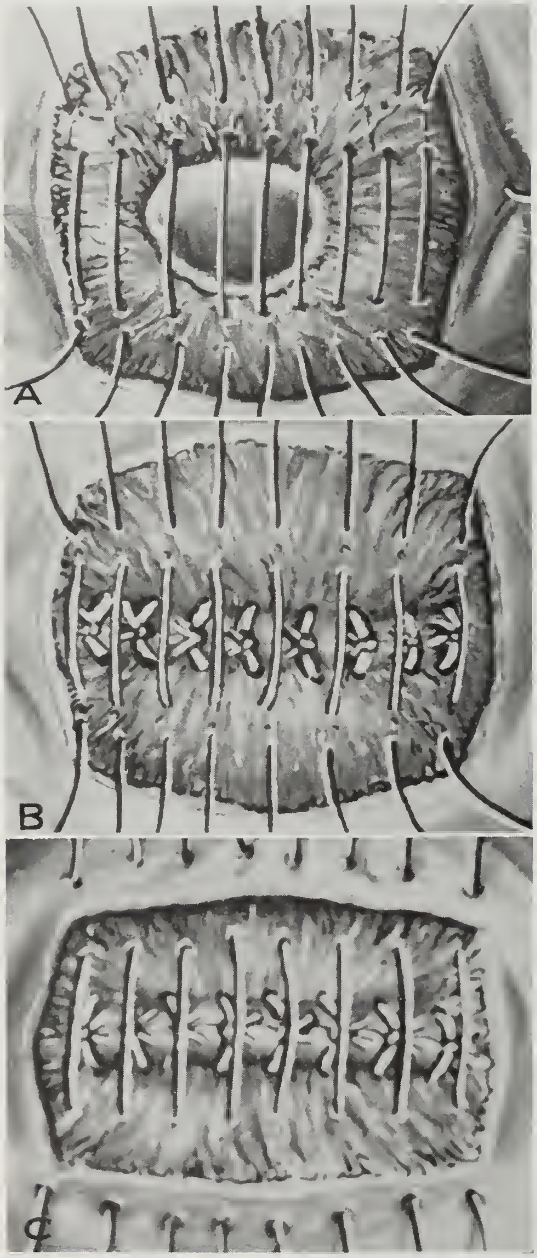

**FIG. 5. A. The first row of interrupted no. 00 chromic catgut sutures has been placed. Several sutures are placed lateral to the fistulous opening. The denuded posterior vaginal wall is used as a flap to cover the fistulous opening. B. The first row of sutures has been tied. A second row of sutures is similarly placed. C. The third row of silver wire sutures approximates the cut mucous membrane edges.**

After the sutures were in place the Foley catheter in the fistula was deflated and removed. After the first row of sutures had been tied the bladder was filled with about 100 c.c. of sterile milk. If any leakage was noted, additional sutures were put in place.[3] When the area was dry, a second row of sutures was put in place (figure 5-B). The vaginal mucosa was then closed with interrupted silver wire sutures (figure 5-C). The mediolateral incision was closed with chromic catgut in a routine manner. Figure 6 shows the final closure.

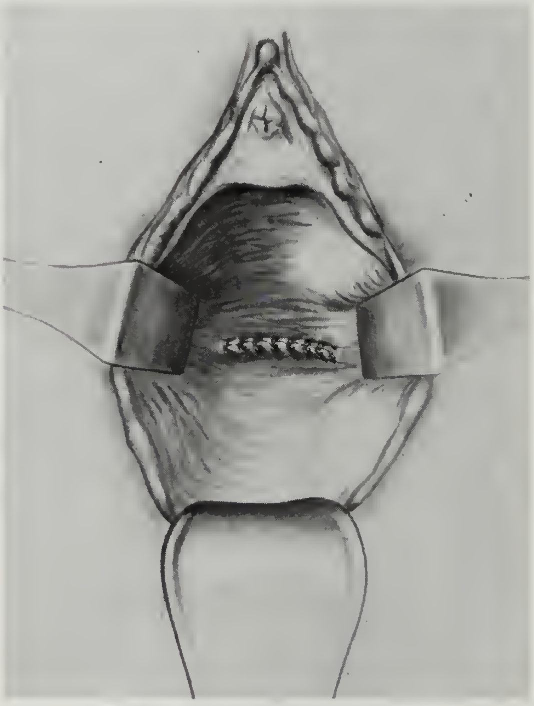

**FIG. 6. Mucous membrane edges of the vaginal vault have been approximated.**

In one case I did not close the vaginal mucosa with silver wire but with chromic catgut, and a great difference was noted in the healing of the vaginal mucosa. Silver wire, besides being nonreactive, also has a bactericidal action. This has been shown on culture plates on which silver wire is placed, and bacteria streaked onto the culture media. For a considerable area around the silver wire no bacterial growth occurs. With silver wire the vaginal mucosal wound was clean and no evidence of tissue reaction was noted. The catgut-closed vaginal mucosa had a great tissue reaction. I shall use silver wire in all future cases when closing the vaginal mucosa.

Postoperatively, a Foley catheter was left in the bladder and the patient continued on the broad-

(*Continued on page 470*)

# A Diagnostic Approach to the Recognition of Subclinical Diabetes Mellitus in Pregnancy*

ALBERTO FORTUNY, M.D.†

**S**OME PREGNANT WOMEN who develop diabetes mellitus late in the childbearing period may exhibit abnormal glucose tolerance during pregnancy as a premonitory sign of diabetes.[1, 2] It has been shown that oral load-testing of glucose tolerance gives a high percentage of abnormal and misleading results, especially in pregnancy.[3, 4] Furthermore, in pregnant women having 2 oral glucose tolerance tests striking differences between the results of the tests performed under identical conditions have been noted.[4, 5, 6] Usually, these differences have been attributed to the variable rate of alimentary absorption in individual patients.

The intravenous glucose tolerance test is a more accurate means of pinpointing those women with abnormal tolerance.[3, 4, 7-18] This clinical study reports the use of the intravenous glucose tolerance test in a selected group of pregnant patients attending the Prenatal Clinic of the Outpatient Department of the Columbia Hospital for Women.

## Method and Material

*Patients.* The study group consisted of 67 pregnant women. Their ages ranged between 16 and 41 years. They were selected by the criteria listed below from all patients attending the Prenatal Clinic. Patients with conditions that influence carbohydrate tolerance, such as chronic liver disease, hyperthyroidism, chronic inflammatory disease, and renal insufficiency were excluded from the study.

*Criteria for patient selection*:

Family history of diabetes mellitus (any of the blood relatives)

Unexplained fetal death (intrauterine, intrapartum, or neonatal)

Previous delivery of large infants (9 pounds or greater)

Borderline elevated blood glucose value in fasting state

Glycosuria during pregnancy

Resistant monilial vaginitis

*Intravenous glucose tolerance test (IVGTT)*:

Twenty-seven patients of the selected group underwent the following procedure:

Fasting blood specimen for baseline glucose determination and to rule out any hyperglycemic state.

Intravenous injection of 25 Gm. of glucose as a 50 per cent solution in distilled water within a period of 2 to 3 minutes. Samples of venous blood were collected at 15-minute intervals from the end of the glucose injection for a total of 4 specimens.

The remainder of the patients in the group underwent similar testing except that they received 20 Gm. of glucose as a 50 per cent solution. Venous blood samples were taken at 30, 60, 90 and 120 minutes for glucose determination.

*Plotting and computations.* The resultant blood sugar values were plotted against time on semilogarithmic graph paper. This gave a straight or nearly straight line as the logarithms of the blood glucose results declined linearly with time.[10, 16, 19-22] The slope of this line permitted the determination in each case of a fractional decay, K, which represented the per cent per minute decrease in blood sugar after the initial rise following the intravenous glucose injection.[3, 12, 14-18] The value of K was computed from the difference between the natural logarithms of any 2 separate points in the slope, A and B, divided by the intervening time in minutes and multiplied by 100 in order to obtain the value as a percentage. The simplified method described by Solomons and Silverstone[18] in the determination of the K values was used. They eliminated the tables of natural logs and arbitrarily selected 2 points in the slope in such a manner that the sugar concentration represented by the first point was twice the concentration at the second point. The only variable to be determined in computing K, then, was the time interval for the glucose level to decline to half of its value.

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$$K = \frac{\text{Log A} - \text{Log B}}{\text{time B} - \text{time A}} \times 100$$

$$\text{Log A} - \text{Log B} = \text{Log}\,\frac{\text{A}}{\text{B}}$$

$$\frac{\text{A}}{\text{B}} = 2 \text{ (if A is twice B)}$$

$$\text{Log}\,\frac{\text{A}}{\text{B}} = \text{Log } 2 = 0.693$$

$$\therefore K = \frac{0.693}{\text{time B} - \text{time A}} \times 100$$

## Results

The most frequent occurrence in the 67 pregnant women, either single or combined with others, was the presence of diabetes in the family history, followed by the previous delivery of large infants, unexplained fetal death, and glycosuria. Resistant moniliasis was not present in any of the patients meeting the other criteria for selection. The absence of this condition in a high risk group for subclinical diabetes suggests that the predisposing factors appear late in the course of diabetes.

The IVGTT was carried out 68 times in 67 patients. Twenty-two patients were studied in the second trimester, 44 in the last trimester, and 1 in the postpartum period. Five of the tests were considered nonvalid since a straight line could not be drawn from the logarithmic values of the glucose concentrations. One of these patients received another test in the last trimester, and valid test results were obtained.

The normal control constant K values accepted for use in this study were those reported by Solomons et al[15] and are shown in table 1.

The computed values of K in our patients were compared to these normal control constant values for K. Abnormal results were found in 33.7 per cent of our patients tested.

The frequency by which the selection criteria found in the patients correlated with normal and abnormal K values is shown in table 2.

**TABLE 1: Normal Control Constant K Values (Solomons et al)**

| Normal Control K Values | Trimester |  |  | Postpartum* | Nonpregnant |
|---|---|---|---|---|---|
|  | 1st | 2nd | 3rd |  |  |
| Mean value of K | 2.37 | 1.88 | 1.86 | 1.53 | 1.63 |
| Lower limit of K | 1.37 | 1.18 | 1.13 | 0.93 | 0.98 |

* Postpartum values are considered as 1 week after delivery.

**TABLE 2: Correlation of Normal and Abnormal K Values with Selection Criteria**

|  | IVGTT (20 Gm.) |  | IVGTT (25 Gm.) |  | Total IVGTT |  |
|---|---|---|---|---|---|---|
|  | Normal | Abnormal | Normal | Abnormal | Normal | Abnormal |
| Total patients | 20 | 15 | 19 | 8 | 39 | 23 |
| Family history | 16 | 12 | 10 | 6 | 26 | 18 |
| Unexplained fetal death | 6 | 5 | 7 | 2 | 11 | 7 |
| Large infants | 4 | 1 | 4 | 6 | 8 | 7 |
| Glycosuria | 2 | 3 | 1 | 3 | 3 | 6 |
| Borderline fasting blood sugar | 0 | 0 | 0 | 2 | 0 | 2 |
| Resistant moniliasis | 0 | 0 | 0 | 0 | 0 | 0 |

The series included 2 patients who were on chlorothiazide at the time that the IVGTT was performed, and both showed abnormal glucose tolerance results. One patient who had been on chlorothiazide which was stopped 1 week prior to the IVGTT later had a normal K value.

Six of the patients who showed abnormal K values during pregnancy have been studied again in the nonpregnant state. A tabulation of these results compared to their previous IVGTT results is shown in table 3. The number of cases restudied are not considered of statistical value. The results reveal that 2 patients' abnormal glucose tolerance returned to normal; 2 others are still questionable since both were taking an oral contraceptive medication. The remaining 2 patients

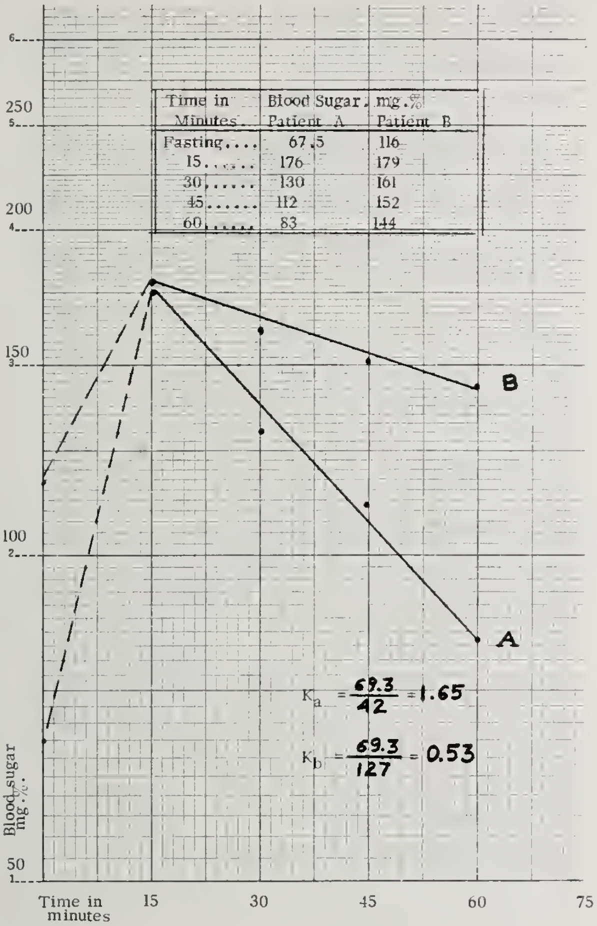
**TABLE 3: Glucose Tolerance Tests on Six Women During and After Pregnancy**

| Patient Code | Initial IVGTT (Pregnancy) |  |  |  |  |  | Follow-up (Nonpregnant) |  |  |  |  |  |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  | Fasting | 15′ | 30′ | 45′ | 60′ | K | Fasting | 15′ | 30′ | 45′ | 60′ | K |
| 1. M. T. | 88 | 150 | 130 | 120 | 113 | 0.66 | 93.5 | 176 | 128 | 116 | 111 | 1.03 |
| 2. L. D.* | 88 | 152 | 138 | 126 | 113 | 0.66 | 103 | 220 | 182 | 154 | 140 | 1.19 |
| 3. D. P.* | 114 | 220 | 182 | 168 | 152 | 0.94 | 110 | 240 | 208 | 176 | 158 | 0.95 |
| 4. S. W. | 116 | 179 | 161 | 152 | 144 | 0.43 | 91 | 192 | 172 | 154 | 131 | 0.86 |
| 5. A. P. | 130 | 210 | 196 | 175 | 171 | 0.56 | 297 | 293 | 284 | 278 | 262 | 0.19 |
| 6. T. P. | 145 | 226 | 213 | 185 | 166 | 0.69 | 199 | 273 | 265 | 254 | 236 | 0.36 |

* Contraceptive medication (Enovid®).

have developed impaired glucose tolerance and are now considered overt diabetics requiring therapy.

The accompanying graph illustrates the plotting and slope of 2 of the patients studied in the series.



| Time in Minutes | Blood Sugar, mg.% Patient A | Patient B |
|---|---|---|
| Fasting.... | 67.5 | 116 |
| 15....... | 176 | 179 |
| 30....... | 130 | 161 |
| 45....... | 112 | 152 |
| 60....... | 83 | 144 |

The K value obtained for patient A, selected only on the basis of a family history of diabetes mellitus, falls into the normal range for the third trimester: 1.65. Patient B, selected because of the family history, previous delivery of large infants, and presence of glycosuria, gave a K value of 0.53. She was first seen close to term, and after induction of labor was delivered of a stillborn 8 lb. 7 oz. fetus. Postmortem examination of the fetus showed great hyperplasia of the islets of Langerhans.

## Discussion

The practical importance of the early diagnosis of subclinical diabetes is that perinatal loss, fetal gigantism, and congenital malformations are increased for a period of several years preceding overt diabetes.[23-36] The embryopathy of an infant born to a mother with subclinical diabetes is similar to that of the infant born to a diabetic mother.[37] More effort should be made to detect these women who are at greater risk with a complicated pregnancy.

When we measured the intravenous glucose tolerance we determined the ability of a particular subject to dispose of blood glucose. Any test in which there is an interference of the glucose absorption will lead to unreliable and misleading results, particularly when time is a significant factor in the interpretation. The intravenous glucose tolerance test was used in order to minimize the errors due to the absorption and time lapse in the oral test.

We have performed the majority of our tests during the second half of pregnancy. Most of the established changes in relation to abnormal carbohydrate metabolism occurring during pregnancy appear at this time. Insulin resistance normally develops as the second half of pregnancy progresses, particularly after 26 weeks.[23] On the other hand, the fasting level of plasma insulin and the insulin released following intravenous injection of glucose have been shown to increase in normal pregnant women from the second half of pregnancy as compared to nonpregnant control groups.[38]

It has also been shown that the intravenous injection of a 50 per cent glucose solution provokes an insulin response and that a correlation between the administered dose and the insulin response does exist.[39] Insulin secretion appears to be a function of the blood sugar level when the pancreatic response is adequate.[40]

If a deficit in insulin response is present a low tolerance index will become clearly evident after an intravenous load of glucose. A number of investigators have examined the effects of various doses upon glucose tolerance by determination of the decay constant K as an index of glucose tolerance. They have presented proof in their publications of the validity of this concept.[13, 41]

This index of glucose tolerance can only be determined reliably if the IVGTT is of short duration and with multiple samples. Since blood sugar values fall to lower limits after 1 to 2 hours alterations will be introduced by other compensatory processes. Homeostasis will tend to add glucose to the circulation. The tolerance test reflects a control response of glucose homeostasis,[13] since glucose tolerance is a function of the extra insulin, above basal, which is normally produced in response to a glucose load.

The intravenous glucose tolerance test has proven to be more reliable in detecting abnormal glucose tolerance among those pregnant patients meeting the criteria for suspected diabetes.

As to the immediate practical significance of an early diagnosis of subclinical diabetes, there is reason to believe that by treating the patient in this early stage, fetal abnormality might be minimized and development of overt diabetes in the mother delayed, perhaps beyond the childbearing age.[42, 43, 44]

## Summary

A preliminary report is presented on the evaluation of the intravenous glucose tolerance test in a selected group of pregnant women. Its expression as an index of tolerance is represented by a decay constant for blood glucose.

Although it has been stated that the diagnosis of subclinical diabetes should be directed to other parameters than abnormal carbohydrate metabolism, at the present time a reliable method of diagnosis is the use of the certain criteria in order to select a high risk group of patients and the use of the intravenous glucose tolerance test in the selected group of pregnant women and continued study of those showing an abnormal index of tolerance.

The incidence of abnormal index of tolerance in our selected group was 33.7 per cent.

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# Congenital Malformations in Offspring of Diabetic Mothers

EDWARD J. CONNOR, M.D.*

THE DIABETIC PREGNANT WOMAN is not only threatened by the possibility of a perinatal fetal loss of 10 to 25 per cent[1-5] but also of an increase of 2 to 3 times of congenital malformation of the infants.[1, 4, 6, 7]

Our experiences with congenital malformations of infants born of diabetic mothers will be discussed, as well as possible reasons for the increased incidence.

Our series includes diabetic pregnant patients from 2 hospitals, Columbia Hospital for Women, where there were 104 deliveries of diabetic pregnant women from 1957 to 1966, and Georgetown University Hospital, where there were 102 deliveries to diabetic pregnant patients between 1949 and 1963.

The definition of congenital malformation used is that of Pedersen et al,[8] which is any structural abnormality present at birth and recognizable by the naked eye, with the exception of the most negligible abnormality. Pedersen classified major congenital malformations as comprising partly the lethal malformations and partly the malformations that are likely to handicap the person seriously throughout life. His definitions are used because of his vast experience in this field. His series included 853 pregnancies in diabetic patients between 1926 and 1963.

In the Columbia series there were 7 congenital defects in the 104 pregnancies. The defects as well as classification of the mothers' diabetic state are listed in table 1. There were 4 major and 3 minor defects. Among the major defects 3 were lethal. In the Georgetown series there were 6 congenital defects in the 102 pregnancies. The defects are listed in table 2.

In table 3 are listed the number and severity of anomalies in the Columbia and Georgetown series compared to those in Pedersen's series. Table 3 also gives similar data presented by Pederson et al[8] and by Eastman and Hellman[9] in infants born of nondiabetic mothers for comparison.

**TABLE 1: Anomalies of Offspring and Diabetic State of Mothers (Columbia Hospital Series)**

| Case No. | Anomalies | Condition of Infants | Age of Mother | White's Classification of Mother |
|---|---|---|---|---|
| 1. | Complete obstruction of left nostril | Good | 19 | B |
| 2. | Mongolism | Good | 41 | C |
| 3. | Deformed fifth toes | Good | 26 | A |
| 4. | Cardiomegaly, hypoplasia of aorta, hypertrophy of pulmonary artery, atresia of left ventricle, hypoplasia of left atrium | Neonatal death | 29 | A |
| 5. | Vestigial thyroglossal cyst | Good | 40 | B |
| 6. | Atresia of distal third of transverse colon, descending colon, rectosigmoid | Neonatal death | 34 | C |
| 7. | Absence of kidneys, adrenals, ureters, bladder; rudimentary left lung | Stillborn | 31 | A |

## Influence of the Severity of the Diabetes on the Type and the Degree of Malformations

White's criteria[10] are a useful method of classifying diabetics. Class A have an elevated postprandial blood sugar, a normal fasting blood sugar, and no need for insulin. Class B had the onset of diabetes after the age of 20 with a duration of less than 10 years and no detectable vascular changes. Class C had no detectable vascular changes, but the diabetes was either of 10 to 19 years' duration, or the onset was between ages 10 and 20 years. Class D had the onset before the age of 10, diabetes of more than 20 years' duration, or retinopathy. Class E had calcification of pelvic vessels. Class F had chronic proteinuria, retinopathy, and nephropathy.

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Whether the severity of diabetes in the mother increases the incidence, type or severity of congenital defects in the infants is a debatable matter. Pedersen[8] believes that there is a predisposition to the cardiovascular and osseous anomalies in severe diabetics (classes D, E and F). Others believe that juvenile diabetics are more apt to deliver offspring with malformations.[11] Driscoll[12] states that there was no apparent correlation of the occurrence of maldevelopment with the severity of the maternal diabetes or its classification. Table 4 lists the results in our combined series as well as Pedersen's series according to White's classification.

**TABLE 4: Incidence of Malformations in Reference to White's Classification of Diabetes**

| White's Classification of Mothers | Pedersen Series | | | Combined Columbia and Georgetown Series | | |
|---|---|---|---|---|---|---|
| | Total No. Infants | Infants with Malformations | | Total No. Infants | Infants with Malformations | |
| | | No. | Per cent | | No. | Per cent |
| A | 62 | 3 | 4.8 | 53 | 4 | 7.5 |
| B | 295 | 15 | 5.1 | 97 | 4 | 4.1 |
| C | 216 | 7 | 3.2 | 49 | 3 | 6.1 |
| D | 238 | 23 | 9.7 | 6 | 2 | 33 |
| E | — | — | — | — | — | — |
| F | 42 | 7 | 16.7 | 1 | — | — |

**TABLE 2: Anomalies of Offspring and Diabetic State of Mothers (Georgetown University Hospital Series)**

| Case No. | Anomalies | Condition of Infants | Age of Mother | White's Classification of Mother |
|---|---|---|---|---|
| 1. | Asymptomatic horseshoe kidney | Good | 33 | B |
| 2. | Bilateral hare lip, cleft palate, congenital absence of right kidney | Good | 33 | D |
| 3. | Hare lip, cleft palate | Died at 1 month of bronchopneumonia | 16 | D |
| 4. | Extra digit, left hand | Good | 36 | A |
| 5. | Hare lip, cleft palate, bilateral clubfeet | Stillborn | 25 | C |
| 6. | Coarctation of the aorta | Stillborn (intrapartum death) | 29 | B |

The reason why infants of diabetic mothers have an increased incidence of congenital malformations is unknown. Many of the theories are conflicting and purely theoretical.

## Various Possible Factors in the Causation of Malformations

*Genetic problems.* Diabetes is a genetically transmitted disease. Therefore, genetic traits associated with diabetes predispose to congenital malformations. However, infants of diabetic fathers and nondiabetic mothers have the same genetic influence, but they do not seem to have an increased incidence of malformations.[8]

*Abnormal intrauterine environment.* The fetus has an abnormal environment because of diabetic changes in the uterine mucosa and changes in the maternal vessels.[8]

*Hyperglycemia.* Hoet[13] believes that insulin deficiencies contribute to the development of congenital defects. In his series there were fewer anomalies when adequate amounts of insulin were employed during pregnancy. Taylor[14] believes that anomalies are related to poor diabetic control in the period just before and shortly after conception.

*Effect of insulin.* It is known that insulin is

**TABLE 3: Statistics of Malformations in Infants Born of Diabetic and Nondiabetic Mothers**

| Series | No. of Infants | Infants with Defects | | Infants with Major Defects | | Infants with Lethal Defects | | Infants with Multiple Defects | |
|---|---|---|---|---|---|---|---|---|---|
| | | No. | Per cent | No. | Per cent | No. | Per cent | No. | Per cent |
| Diabetic Mothers: | | | | | | | | | |
| Georgetown | 102 | 6 | 5.9 | 5 | 4.9 | 1 | 0.98 | 2 | 2.0 |
| Columbia | 104 | 7 | 6.7 | 4 | 3.8 | 3 | 2.9 | 4 | 3.8 |
| Combined Georgetown-Columbia | 206 | 13 | 6.3 | 9 | 4.4 | 4 | 1.9 | 6 | 2.9 |
| Pedersen et al[8] | 853 | 55 | 6.4 | 44 | 5.2 | 18 | 2.1 | 14 | 1.6 |
| Nondiabetic Mothers: | | | | | | | | | |
| Pedersen et al[8] | 1,212 | 26 | 2.1 | 14 | 1.2 | 4 | 0.3 | 3 | 0.2 |
| Eastman[9] | — | — | 2.5 | — | 1.1 | — | 0.5 | — | — |

teratogenic in animals.[15] However, anomalies have an increased incidence in class A diabetics who are not treated with insulin.

*Hypoglycemia.* Reis[16] has related a lower incidence of congenital malformations in his series to moderate glycosuria that he permits in pregnancy. However, many series have a significant number of patients that have had severe insulin reactions without developing anomalies.

*Hyperadrenocorticism.* Both the amniotic fluid and the urine of infants born to diabetic mothers have increased titers of corticoids.[17] There may be some association with increased steroid levels and anomalies. Fraser[18] has found that by treating certain strains of rats with cortisone he would have an increased incidence of defects.

*Placenta insufficiency.* Placental lesions have been described which may impair placental transfer in diabetic gestation.[19]

*Pituitary influence.* Growth hormone is thought to influence excessive fetal growth which may be seen in diabetic pregnancies. Possibly, growth hormone causes hormonal or enzymatic changes that may result in anomalies.[20]

## Prevention of Malformations

There is no known method at the present time to prevent congenital malformations in offspring of diabetic mothers. However, it is desirable to have meticulous diabetic control with frequent visits to the physician. Urine and blood sugar tests should be done frequently to detect acidosis. Hypoglycemia is not consistent with good diabetic management and should be avoided, especially in early pregnancy.

## Discussion

There is a 2- or 3-fold increase in congenital defects in infants born to diabetic mothers. The incidence of minor congenital anomalies is not increased as much as are the major and the lethal defects. There is no consistent type of defect found in these infants as there is in rubella. There was only 1 juvenile diabetic in our series that had an infant with a congenital anomaly. The association between the severity of the diabetes as related to White's classification and the severity and type of congenital defect is uncertain. There were 2 class A diabetics in our series that had babies with lethal defects.

## Summary

Both the Columbia Hospital and Georgetown University Hospital series had an increased incidence of defects in the offspring of diabetic mothers.

The defects were usually of the major variety, but there was no definite type of anomaly.

Theories as to why there is an increased tendency to malformations are listed, but there is no definite cause known.

There is at present no known way to prevent the defects.

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# Second Thoughts on Mammography

MARTIN A. THOMAS, M.D.,* AND EUGENE J. McDONALD, M.D.†

In 1960 Egan[1] published a new technique for making breast X-ray examinations, and using this technique without any clinical information he correctly diagnosed 238 of 245 carcinomas preoperatively for a true positive‡ cancer detection rate of 97 per cent.

In 1961 we began to offer mammography as a routine aid in the diagnosis of breast diseases at Columbia Hospital for Women and have now examined over 3,500 patients.

In a report of our first year's experience[2] we correctly diagnosed 25 of 29 carcinomas for a true positive rate of 86 per cent. The series was very small, and we used clinical information freely before we arrived at a diagnosis.

We were encouraged by our first year's work and decided to continue the mammography program. However, as our experience increased we gradually came to realize that we not only could not attain the high rate of accuracy reported by Egan but that we could not reproduce the accuracy of our own first year of work.

We found that some large carcinomas cannot be demonstrated on the films at all. Many films demonstrated ill-defined opacities which failed to show classic features of either a carcinoma or a benign mass. In other words, many mammograms were in a "gray" area, and their interpretation was quite subjective, if not intuitive. We were continually troubled by the dense, almost opaque, breast tissue of patients who had little radiolucent fat in their breasts.

That others in the country were having similar difficulties became apparent when a national reproducibility study reported a true positive cancer detection rate of 79 per cent.[3]

A combined study in the 7 Philadelphia teaching hospitals[4] reported a true positive rate of 55 per cent in the 40 to 54 age group. They also reported a true positive rate of 52 per cent in those patients clinically categorized as having a "dominant mass not obviously carcinoma."

The results of both of the above studies were generally attributed to poor quality films being interpreted by inadequately trained radiologists. However, we were not convinced that these results could be so easily dismissed.

In coöperation with the Cancer Control Division of the Public Health Service we arranged to have Dr. Egan, the developer of the technique, read films of 250 patients at our hospital who had biopsies. The patients for this study were not consciously selected in any way. Our sole aim was to obtain radiologic-pathologic correlation on 250 patients as quickly as possible.

While we were in the midst of our series Rogers, Powell and Egan[5] reported among other things an overall 70 per cent true positive rate for Egan on films from his own hospital which he read without clinical information. In patients with stage I cancer who were under 50 years of age he correctly diagnosed only 13 of 41 for a 32 per cent true positive rate. However, in patients over 50 with stage II or stage III cancer his true positive rate was 95 per cent.

Of the 250 studies we sent to Dr. Egan 59 were proven carcinomas, and 191 were benign lesions. He correctly diagnosed only 29 of the 59 carcinomas. Of the 191 benign lesions he correctly diagnosed 179 but incorrectly diagnosed 13 as carcinomas. Our accuracy rate was somewhat better, as we correctly diagnosed 36 of the 59 carcinomas and called 12 of the benign lesions carcinoma. The results on a percentage basis are tabulated below.

| | True Positive* Per cent | False Positive† Per cent |
|---|---|---|
| Egan | 49 | 6.8 |
| Columbia Hospital | 61 | 6.2 |

* For definition see column at left.

† False positive rate is the percentage of nonmalignant lesions diagnosed as cancer by X-ray examination preoperatively.

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‡ True positive rate is the percentage of proven cancers correctly diagnosed by X-ray examination preoperatively.

Our film quality cannot be blamed for these results. Dr. Egan stated that "All in all considered, the films are of good quality; my interpretation of them does not detract from that quality."

We have found mammography to be an insensitive cancer detection procedure except in older patients or in those with large lesions. The great majority of our patients are below 55 years of age, and we rarely had the opportunity to make films on a patient with advanced cancer.

In view of our experience we must ask ourselves if it is worth while to continue mammography. The answer to this, in our opinion, is yes. While we have missed a high percentage of cancers, we have also confirmed that some nonpalpable carcinomas can unequivocally be demonstrated by X-ray examination. In an older patient with large breasts the mammogram can more surely help us diagnose the presence of a small cancer than can palpation. We recommend mammography for highly motivated patients in high-risk categories, such as those from "cancer families" or those who have had a previous mastectomy. These patients have a better chance of being the fortunate individuals in whom a cancer might be detected before it becomes palpable.

While a negative mammogram should never deter the surgeon from exercising his clinical judgment in regard to an indeterminate breast mass, a positive mammogram may serve to expedite the proper therapy. Rarely, the preoperative mammogram may point to an area of suspicion in another location in the same breast or in the opposite breast. In those patients who have breast symptoms such as pain or nipple discharge and who have no mass, mammography has given reassurance to the surgeon and helped him assuage the pangs of cancerophobia.

Six years and 3,500 patients have also taught us the absolute necessity of excellent film technical quality and an experienced thorough film reader. Films of poor technical quality make an insensitive study to begin with quite pointless. Even the best of films cannot be read casually but must be studied with the utmost care.

There is now increasing pressure from the lay public and from the Cancer Society to institute routine mammography screening of large population groups. Our experience shows that mammography is not yet, and may never be, a practical screening tool. Review of large-scale mammogram surveys done by others to date shows an average cancer pick-up rate of 1.7 per 1,000 patients on the first pass through the group. This pick-up rate decreases on subsequent screening of these groups. Experience has shown that one must do biopsies on 4 or 5 patients with suspicious mammograms to obtain 1 cancer. We also know from these studies that about half of the cancers in asymptomatic patients will not be picked up at all by mammography. However, it is significant to note that only 15 per cent of the patients with cancer picked up in this manner had positive nodes.

A realistic opinion is that periodic mammography screening holds little or no promise for mass effectiveness, primarily because of the low yield. There is also difficulty in motivating patients to continue with the serial examinations, and then there are difficulties in getting patients to submit to biopsy if they turn up with a suspicious mammogram. Less important but significant deterrents to implementation of a mass-screening program include the cost of producing the films and finding qualified people to interpret them. However, for the patient who is highly motivated, mammography every year or two should significantly increase the chances that a tumor will be detected earlier and in a more curable stage than if the patient is left to find it herself.

We have found that mammography can stimulate interest in breast disease within the medical community and that it gets surgeons, pathologists, and radiologists working together as a team. This has resulted in a decrease in the average size of a tumor at the time of biopsy, along with an increase in the percentage of positive biopsies. There is every reason to believe that this, in turn, results in a higher cure rate.

## Summary

After 3,500 patient examinations over a 6-year period we conclude that mammography is relatively insensitive as a cancer detection procedure.

We report a true positive cancer detection rate of 61 per cent with 6.2 per cent false positive diagnoses in a series of 250 unselected patients with biopsies. The films of these patients were read as part of a double blind study by Dr. Robert Egan, developer of the technique currently in vogue. He correctly diagnosed 49 per cent of the carcinomas and called 6.8 per cent of the benign lesions carcinoma.

Mammography, however, can demonstrate nonpalpable carcinomas. It can detect 1.7 carcinomas per 1,000 asymptomatic patients.

Mammography in conjunction with clinical examination seems to result in a higher percentage of positive biopsies, smaller tumor size at biopsy, and a smaller percentage of positive nodes.

Mammography seems to accomplish this by increasing interest in breast cancer detection among patients and by leading to better team work between clinicians, radiologists, and pathologists.

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### Repair of Vault Vesicovaginal Fistula—Sheffery

(*Continued from page 460*)

spectrum antibiotics. The cortisone was discontinued. Contrary to others, I left the catheter in for 10 days, at which time it was removed. The day it was removed the patient was encouraged to void every hour for the first 24 hours, every 2 hours for the second 24 hours, and every 3 hours for the third 24 hours.

On the fourth day after the catheter had been removed (the fourteenth postoperative day) the patient was returned to the operating room where under anesthesia the wire sutures were removed. The bladder was again filled with sterile milk solution to see if there was any leakage. If all was well the patient was discharged the following day.

All 3 patients have been symptom-free with no leakage of urine for over 1 year. I believe that successful management of these cases depends on meticulous attention to the most minute details of care, both pre- and postoperatively, and an unhurried, careful dissection and surgical repair.

Grateful acknowledgment is made to Henry C. Falk, M.D., New York, N.Y., and to the F. A. Davis Company, Philadelphia, for the use of the illustrations in this paper which appeared originally in the book, "Urologic Injuries in Gynecology."

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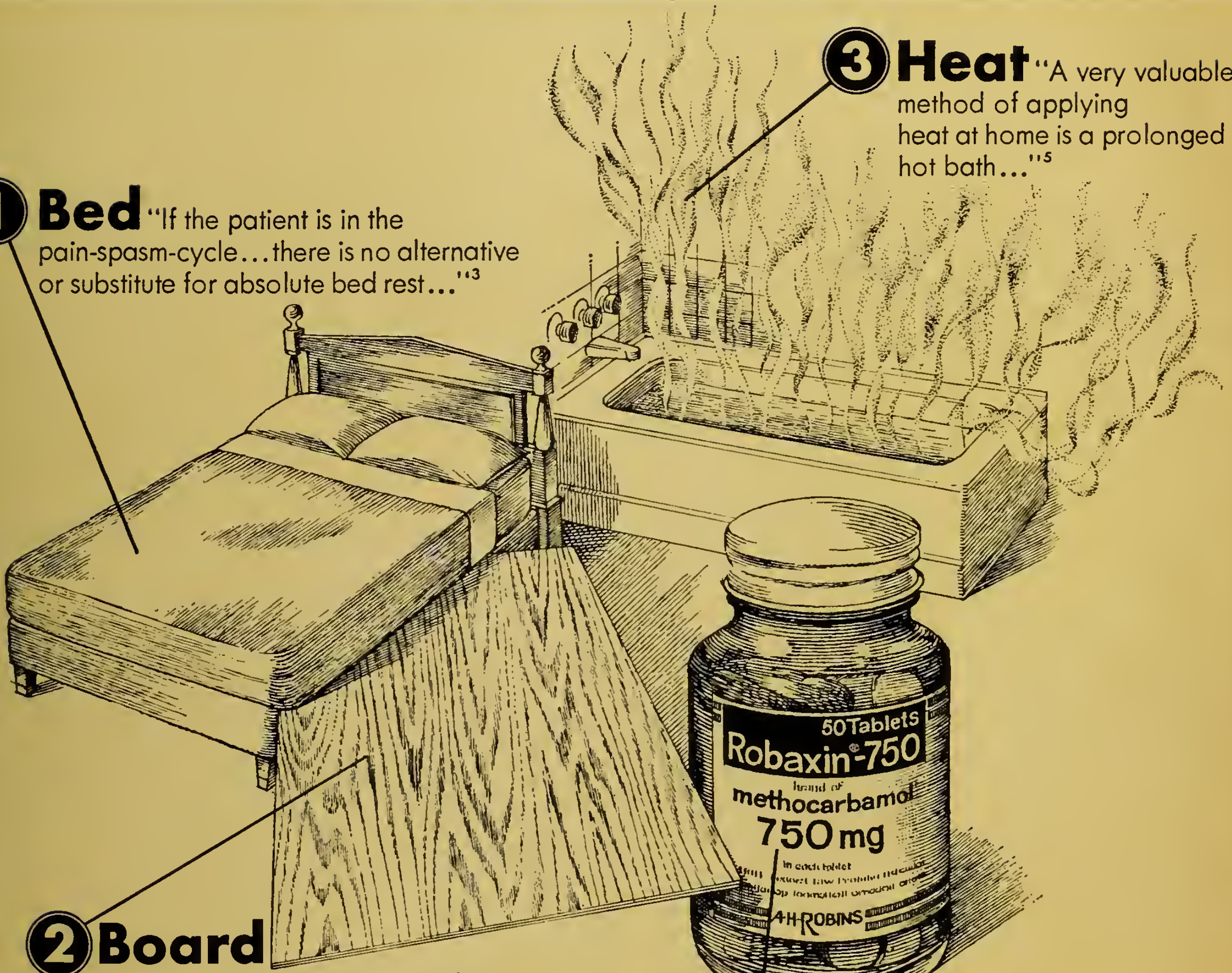
# LOW-BACK PAIN

## A CONSERVATIVE, FOUR-POINT PROGRAM

**The low back pain that is most frequently seen in general practice is mechanical in nature, i.e., postural back pain, joint dysfunction and acute back strain.[1,2] For this type of discomfort, a conservative regimen is usually sufficient to relieve aches and pains, and to help keep the patient functioning. Components of this basic program include:**



**① Bed** "If the patient is in the pain-spasm-cycle... there is no alternative or substitute for absolute bed rest..."[3]

**② Board** "Boards should be ordered under the mattress... these boards act by immobilizing the spine..."[4]

**③ Heat** "A very valuable method of applying heat at home is a prolonged hot bath..."[5]

**④ Robaxin®-750** (methocarbamol, 750 mg. capsule-shaped tablets) A well-tolerated[6] skeletal muscle relaxant, methocarbamol helps relieve spasm "...without interfering with normal tone and movement."[7] And there is little likelihood of sedation.[6]

Indicated for relief of skeletal muscle spasm. **Contraindicated** in hypersensitive patients. **Side Effects** (lightheadedness, dizziness, drowsiness, nausea) may occur rarely, but usually disappear on reduced dosage. Hypersensitivity reactions develop infrequently. See product literature for further details. **Also available:** Robaxin® Tablets (methocarbamol, 500 mg.) Robaxin Injectable (methocarbamol, 1 Gm./10 cc.) **References:** (1). Godfrey, C.M.: Applied Therap. *8*:950, 1966. (2). Gottschalk, L.A.: GP *33*:91, 1966. (3). Rowe, M.L.: J. Occup. Med. 2:219, 1960. (4). Cazen, L.: South Dakota J. Med. *18*:26, 1965. (5). Sato-Hall, R.: Med. Sc. *14*:23, 1963. (6). Weiss, M. and Weiss, S.: J. Am. Osteopath. A. 62:142, 1962. (7). Feuer, S.G., *et al.*: New York J. Med. 62:1985, 1962.

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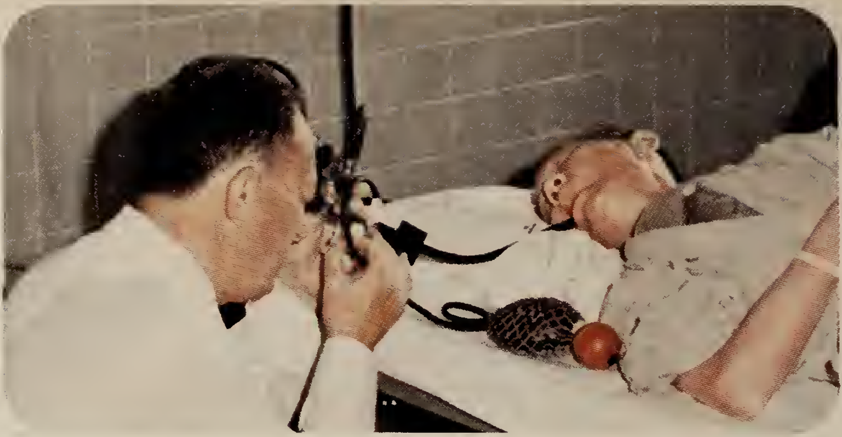
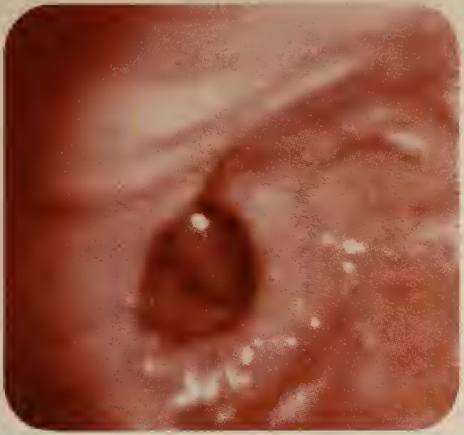


NEW EVIDENCE:

**Pro-Banthīne®** (propantheline bromide) **gives positive, selective benefits in gastrointestinal disorders.**



Intragastric photograph of pyloric region showing complete relaxation of pyloric sphincter with 6 mg. of Pro-Banthīne intravenously.

AN IMPORTANT PROBLEM in managing gastrointestinal disorders has been the choice of an anticholinergic agent which will act positively and selectively on the gastrointestinal tract without extensive secondary effects.

Recent direct observations with the cinefibergastroscope and intragastric photography[1] visually confirm previous evidence that Pro-Banthīne does, indeed, possess such selective activity.

Barowsky and his associates demonstrated that a minimal dose of 6 to 8 mg. of Pro-Banthīne intravenously produced complete relaxation of gastric activity. Secondary effects were not significant.

By contrast, it required 0.8 mg. or double the usual dose of atropine intravenously to achieve similar gastric relaxation. Side effects of this dosage of the belladonna alkaloid were pronounced. Ventricular rates were as high as 150 per minute.

For positive, selective anticholinergic benefits Pro-Banthīne is indicated in patients with peptic ulcer, gastritis, irritable colon and other forms of gastrointestinal hypermotility.

**Dosage:** The maximal tolerated dosage is usually the most effective. For most *adult* patients this will be four to six 15-mg. tablets daily in divided doses. In severe conditions as many as two tablets four to six times daily may be required. Pro-Banthīne (brand of propantheline bromide) is supplied as tablets of 15 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type ampuls of 30 mg. The parenteral dose should be adjusted to the patient's requirement and may be up to 30 mg. or more every six hours, intramuscularly or intravenously.

**Contraindications:** In glaucoma or severe cardiac disease.

**Precautions:** Since varying degrees of urinary hesitancy may occur in the elderly male with prostatic hypertrophy, this should be watched for in such patients until they have gained some experience with the drug.

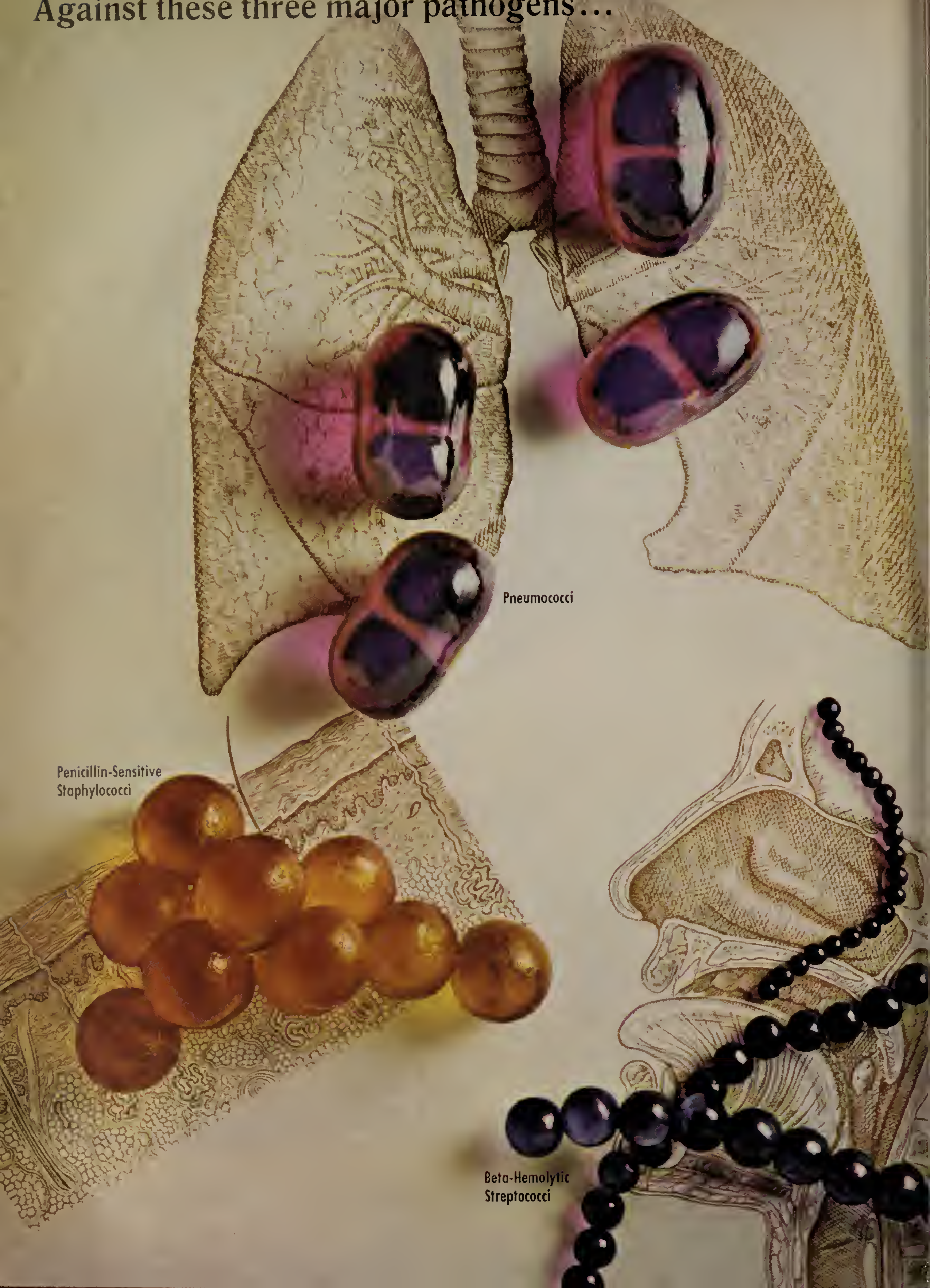
Although never reported, theoretically a curare-like action may occur with possible loss of voluntary muscle control. Such patients should receive prompt and continuing artificial respiration until the drug effect has been exhausted.

**Side Effects** The more common side effects, in order of incidence, are xerostomia, mydriasis, hesitancy of urination and gastric fullness.

[1] Barowsky, H.; Greene, L.; Bennett, R., and Buganza, G.: The Effect of Anticholinergic Drugs on Gastric Motility and Pyloric Function, Scientific Exhibit, Annual Convention of the American Medical Association, Chicago, Illinois, June 26-30, 1966.

SEARLE *Research in the Service of Medicine*

# Against these three major pathogens...


Pneumococci
Penicillin-Sensitive Staphylococci
Beta-Hemolytic Streptococci

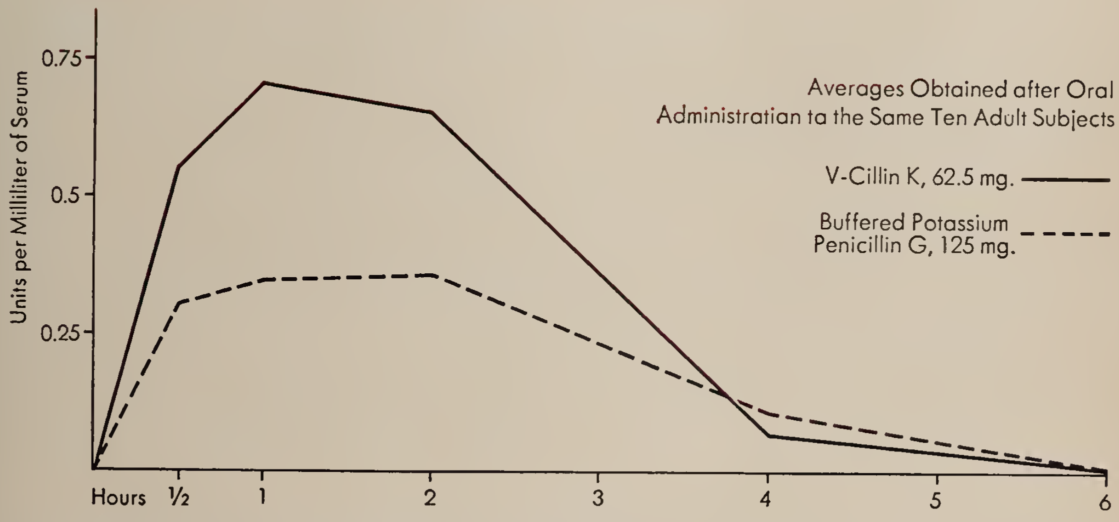
# V-Cillin K® provides dependable oral antibacterial activity

## because it combines a high degree of in-vitro activity...

| Antibiotic | Staph. Aureus (Penicillin-Sensitive) MIC (mcg./ml.) Median | Range | Streptococcus, Group A MIC (mcg./ml.) Median | Range | Diplococcus Pneumoniae MIC (mcg./ml.) Median | Range |
|---|---|---|---|---|---|---|
| Penicillin V | 0.02 | 0.02-0.04 | 0.02 | 0.003-0.4 | 0.01 | 0.005-0.2 |
| Penicillin G | 0.02 | 0.005-1.6 | 0.005 | 0.002-0.2 | 0.02 | 0.01-0.1 |
| Methicillin | 1.6 | 0.4-6.3 | 0.2 | 0.1-0.4 | 0.2 | 0.1-1.6 |
| Oxacillin | 0.4 | 0.1-3.1 | 0.04 | 0.02-0.4 | 0.1 | 0.04-0.8 |
| Cloxacillin | 0.2 | 0.2-0.8 | 0.1 | 0.1-0.8 | — | — |
| Nafcillin | 0.4 | 0.2-0.8 | 0.04 | 0.02-0.1 | 0.02 | 0.02-0.2 |
| Ampicillin | 0.2 | 0.1-0.8 | 0.02 | 0.01-0.04 | 0.02 | 0.01-0.04 |

Adapted from Klein, J. O., and Finland, M.: New England J. Med., 269:1019, 1963.

## with high blood levels, even in the presence of food



Adapted from Griffith, R. S., and Black, H. R.: Current Ther. Res., 6:253, 1964.

**V-Cillin K®** Lilly 700867

**Potassium Phenoxymethyl Penicillin**

*(See next page for prescribing informatio*

# New 500 mg. tablets...a more convenient way to give high doses

100
No. 1832
V-CILLIN K®
POTASSIUM PHENOXYMETHYL PENICILLIN TABLETS, U.S.P.
500 mg. (800,000 Units)
DATED
Lilly

**Description:** V-Cillin K is the potassium salt of V-Cillin® (phenoxymethyl penicillin, Lilly). This chemically improved form combines acid stability with immediate solubility and rapid absorption. Higher serum levels are obtained more rapidly with this penicillin than with equal oral doses of penicillin G. The higher serum levels and acid stability of V-Cillin K make it a more dependable penicillin for oral use.

V-Cillin K, Pediatric, is an oral solution of clinically proved V-Cillin K in teaspoon dosage form. When mixed as directed, each 5 cc. (approximately one teaspoonful) will contain 125 mg. (200,000 units) phenoxymethyl penicillin as the potassium salt.

**Indications:** V-Cillin K has been shown to be effective in the treatment of streptococcus, pneumococcus, and gonococcus infections as well as infections caused by sensitive strains of staphylococci. It may be used for the prophylaxis of streptococcus infections in patients with a history of rheumatic fever and for the prevention of bacterial endocarditis after tonsillectomy and tooth extraction in those patients with a history of rheumatic fever or congenital heart disease.

**Contraindication:** V-Cillin K should not be administered to a patient with a history of penicillin hypersensitivity.

**Warnings:** In rare instances, the use of penicillin may cause acute anaphylaxis which may prove fatal unless promptly controlled. This type of reaction appears more frequently in patients with a history of sensitivity reactions to penicillin and in those with bronchial asthma or other allergies. Resuscitative drugs should be readily available for emergency administration. These include epinephrine and pressor drugs (as well as oxygen for inhalation) for relief of immediate allergic manifestations and antihistamines and corticosteroids for delayed effects.

**Precautions:** V-Cillin K should be used cautiously, if at all, in a patient with a strongly positive history of allergy.

In prolonged therapy with penicillin, and particularly with hig parenteral dosage schedules, frequent evaluation of the renal an hematopoietic systems is recommended.

In suspected staphylococcus infections, proper laboratory studie (including sensitivity tests) should be performed.

The use of penicillin may be associated with the overgrowth c pencillin-insensitive organisms. In such cases, its administration shoul be discontinued, and appropriate measures should be taken.

**Adverse Reactions:** Although serious allergic reactions are much les common with administration of oral penicillin than with intramusculc forms, manifestations of penicillin allergy may occur.

Penicillin is a substance of low toxicity, but it does possess a signi cant index of sensitization. The following hypersensitivity reactior associated with the use of penicillin have been reported: skin rashe ranging from maculopapular eruptions to exfoliative dermatitis; ur caria; and reactions resembling serum sickness, including chills, feve edema, arthralgia, and prostration. Severe and often fatal anaphylax has occurred (see Warnings). Hemolytic anemia, leukopenia, thror bocytopenia, and nephropathy are rarely observed side-effects ar are usually associated with high parenteral dosage.

**Administration and Dosage:** For Tablets V-Cillin K and for V-Cillin Pediatric, the usual dosage ranges from 125 mg. (200,000 units) thre times a day to 500 mg. (800,000 units) every four hours. For infant the daily dosage may be 50 mg. per Kg. of body weight divided in three doses.

Beta-hemolytic streptococcus infections without associated ba teremia may be treated with 200,000 to 400,0000 units three times day. Therapy should be continued for a minimum of ten days to preve development of rheumatic fever and/or other serious complicatior Dosage for routine streptococcus prophylaxis in patients with a histo of rheumatic fever or congenital heart disease may be 200,000 un once or twice daily. When such patients undergo tonsillectomy, too extraction, or other minor surgery, the prophylactic dose should l 500,000 units every six hours given two days prior to surgery and f two days postoperatively. If oral medication is not feasible on the d of surgery, parenteral therapy should be considered. Mild to mode ately severe pneumococcus pneumonia has been treated effective with 250 mg. every six hours.

In staphylococcus infections, 400,000 units or more should be giv every six to eight hours in conjunction with indicated surgical proc dures.

For gonorrhea in males, 500 mg. (800,000 units) every four hours f three doses may be employed; in females, 500 mg. every four hou for six doses are recommended. Refractory infections generally respo to a second treatment three to four days following completion of t first. Treatment of gonorrhea with severe complications should individualized, with prolonged and intensive treatment. Patients wit suspected lesion of syphilis should have a dark-field examination t fore receiving penicillin and monthly serologic tests for a minimum three months.

**How Supplied:** Tablets V-Cillin K, U.S.P., 125 mg. (200,000 units), bottles of 50 and 100; and 250 mg. (400,0000 units) and 500 n (800,000 units), in bottles of 24 and 100.

V-Cillin K, Pediatric, for Oral Solution, 125 mg. (200,000 units) p 5 cc. of solution, in 40, 80, and 150-cc.-size packages. [0320

*Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana 46206.*

# PRESIDENT'S PAGE

## THE MEDICAL SOCIETY AND DOCPAC

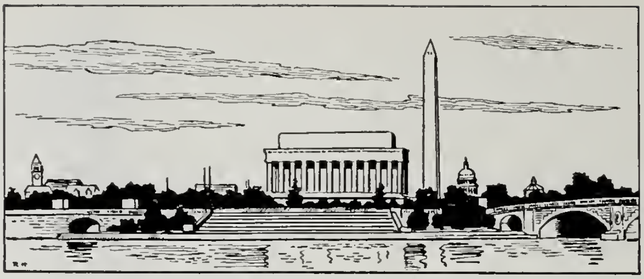
It occurs to me that there may be some discussion regarding the attitude of the Medical Society of the District of Columbia in relation to the District of Columbia Political Action Committee (DOCPAC). This message is an effort to clarify the situation.

The original act of incorporation of the Medical Society of the District of Columbia, approved by the Congress of the United States, February 16, 1819, signed by President James Monroe, and "revived with amendments," July 7, 1838, and again May 24, 1924, likewise approved by Congress and signed by Presidents Martin Van Buren and Calvin Coolidge, respectively, states that the "body" is constituted "for the purpose of promoting and disseminating medical and surgical knowledge, . . ." Article II of Chapter I of our Constitution and By-laws reads: "The object of this Society shall be the promotion of the science and art of medicine, sanitation and the common interests of its members and the public." DOCPAC was organized and is dedicated to the promotion of participation by physicians in strictly nonpartisan political activity. The areas of interest, therefore, of these 2 groups are not antagonistic; by the same token they are oriented in significantly different channels. It is my conviction that these purposes should remain separate and distinct. They should not be merged—by direct collaboration or by inference. The Medical Society should limit its activities to those areas specified in its incorporation and spelled out in its Constitution. DOCPAC must accept the responsibility of standing on its own feet to achieve its commendable objectives.

DOCPAC has requested concurrent billing with Medical Society dues. This request has been denied. Refusal was based primarily on the theses mentioned above. My position is that such action would imply an obligation on the part of a member to join DOCPAC, and further would indicate direct sponsorship of DOCPAC by the Medical Society. Such interpretation does not reflect the facts of the matter. I submit that the Medical Society is a professional and scientific organization only. DOCPAC is the medium through which physicians can participate in political activity.

Physicians generally are outstanding citizens, and should assume a more active role in civic and community affairs at all levels. The organization developed to augment effectiveness in the political arena is DOCPAC. You are urged to offer your support.

Henry D. Ecker



# EDITORIALS

## Columbia Hospital—A Record of Service to Women

Columbia Hospital for Women, one of less than a dozen such specialty hospitals remaining in the Nation, has achieved a significant record of professionalism during its 101 years of service. Having survived the trend to close limited hospitals, Columbia now looms as the maternity hospital for Metropolitan Washington.

Founded in 1866 to provide care for the hundreds of women stranded in Washington following the Civil War, Columbia Hospital was given a charter by Congress to treat diseases peculiar to women and to serve as a lying-in asylum. It has been a pacemaker during the past century in the development of delivery room techniques, the lowering of mortality rates, and in providing many "firsts" in the march of medicine.

Its clinic for children became the forerunner of Children's Hospital. It instituted the first program of prenatal care in the country, and its prenatal clinic served as a model for other institutions. The Hospital established one of the first premature nurseries in the Nation, taking the lead in insuring better care for premature babies as well as improved isolation facilities for infected infants.

With the assistance of the FBI Columbia established the first footprint identification system as a part of hospital records—a program which has also served as a model for other hospitals. It was the first hospital to conduct classes for expectant fathers. It also took the lead with the early establishment of a recovery room.

Many of the modern standards and procedures of medical practice were initiated at Columbia. Its policies and programs have served as a guide to hospitals throughout the Nation and in foreign countries. The rosters of the board and professional staff have listed the names of some of the Nation's most distinguished citizens and physicians, including 2 United States Presidents.

In 1903 Dr. Truman Abbe, of Columbia's staff, returned from the Curie Clinic and used radium therapy for the first time in the U.S.A.[1] The routine use of a recovery room for postoperative patients started a system which was to be accepted widely.

During his residency at Columbia in 1920 Dr. Joseph Kreiselman observed the need for immediate resuscitation of the newly born, and the machine he devised at that time has become standard delivery room apparatus. After World War I, under urging by the staff, the Anesthesia Department established round-the-clock coverage for obstetrics.

As the Hospital begins its second century of community service, Columbia is now in the process of conducting an extensive survey in an effort to anticipate future requirements of the Hospital to meet the needs of the community. The E. D. Rosenfeld Association, Inc. is making a thorough study of the present facilities of the Hospital and its possible future expansion.

Columbia has recently agreed to a teaching affiliation in obstetrics and gynecology with the George Washington University School of Medicine. In conjunction with the University-affiliated program, a full-time Director of Medical Education has been appointed by the Hospital to supervise the residency training at Columbia.

An equally important affiliation has just been completed between Georgetown University and the Pediatrics Department of Columbia. The aim is to improve residency coverage of the Pediatrics Department and to institute the latest improvements in available intensive care treatment of newly born infants.

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[1] Abbe, T.: Notes on the physiologic and the therapeutic action of radium. Washington Med. Ann., 1904, 2, 363.

*Opinions expressed in contributions to the Editorial Section are those of the writers and do not necessarily reflect the views of the Medical Society of the District of Columbia*

Development of special research projects is also planned as Columbia moves forward in its programs for the future.

As Washington's only hospital exclusively for women, Columbia stands on the threshold of providing many new service concepts in the field of obstetrics and gynecology.

Stafford W. Hawken, M.D.
*Chief of Staff, Columbia Hospital for Women*

## Use of Packed Red Cells

From the standpoint of maximum patient benefit and economy of blood, whole blood and its component parts respectively must be properly utilized. It is generally recognized that whole blood should be used primarily in the treatment or anticipation of further acute blood loss when it is necessary to restore or maintain the blood volume as well as the oxygen-carrying capacity.

Packed red cells supply the oxygen-carrying capacity of whole blood with about one-half its volume and are preferable in most other situations where blood is needed. This is particularly true in patients with chronic anemia who are not hypoproteinemic, in patients with associated cardiac or renal problems where edema is present or impending, and in the elderly.

There are a number of things to be gained by the use of packed red cells. These include:

1. In many instances, particularly in the elderly or when large amounts of blood need be given, one can reduce the danger of overloading the circulation leading to heart failure and pulmonary edema by using blood from which most of the plasma is removed.

2. The transfusion of proteins, antibodies, or other substances contained in plasma may cause an anaphylactic or allergic reaction. There are other plasma sensitivity reactions which may occur, particularly in patients who have chronic disorders and need to be transfused repeatedly. These can often be avoided by the use of packed red cells.

3. By using packed red cells one frees the residual plasma for the fractionation and the preparation of serum albumin, gamma globulin, fibrinogen, platelets for transfusion in leukemia, thrombocytopenia, etc., and cryoprecipitates in the treatment of hemophilia. These are substances which are in increasing demand, and much greater utilization can thus be made of blood and blood products.

Finally, the transfusion of blood or its components should never be undertaken unless a serious disturbance is created by its loss or lack. "With this form of therapy, as with any other, it is important to know the conditions that require its use, to understand what can and cannot be accomplished by transfusion, and especially to weigh the possibility of injury against the anticipated benefit. The skillful use of blood transfusion requires all these plus thoughtful consideration of each patient and his need."

Medical Advisory Committee
*District of Columbia Chapter, American Red Cross*

## Editor of Oldest Medical Journal Retires

Dr. Joseph Garland, Editor of *The New England Journal of Medicine* since 1947, retired, July 1; his successor is Dr. Franz J. Ingelfinger, formerly Professor of Medicine at Boston University. In the *New England Journal* of June 22, an editorial, entitled "Chain of Responsibility," which must represent the epitome in modesty, announced Dr. Ingelfinger's succession as editor with no reference to Dr. Garland's long tenure. It can be assumed therefore that Dr. Garland wrote it. He never initialed or identified his own or other editorials in his *Journal.*

The *Medical World News* of June 23 carried a warm and appreciative story of Dr. Garland's life and his many contributions to the field of medicine, particularly to the literature. The article, most appropriately headed, "Leaving an Indelible Imprint on Medicine," is well worth reading. The same issue contained a brief and interesting history of the *Journal*, referred to as "the prestigious 155-year-old publication," whose ancestry can be traced back in direct line to a quarterly publication founded in 1812 by 2 Boston physicians.

Dr. Garland will be greatly missed for his inimitable editorials and for the style and innovations he brought to his *Journal.* He will also be

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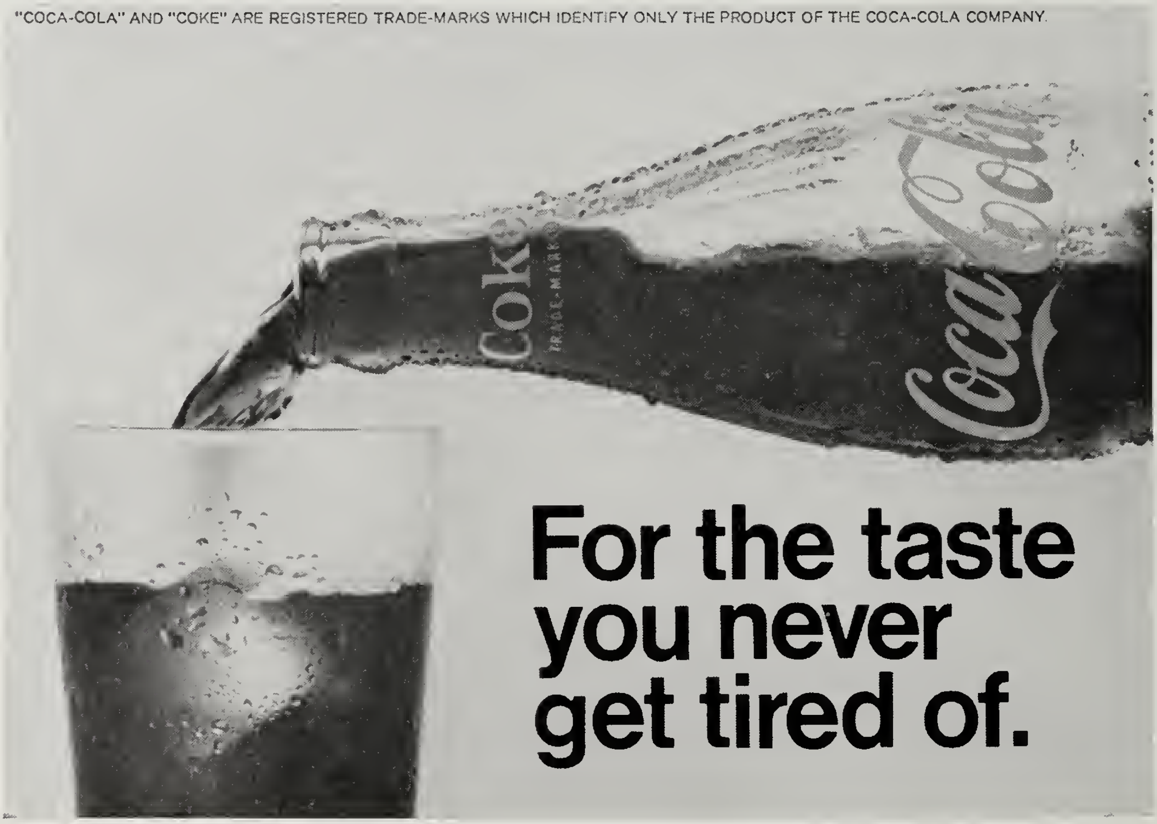
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missed by those of us in the State Medical Journal Group who had the opportunity and privilege many times to hear him speak on editorial matters at our biennial meetings.

To "one of the century's most creative editors," the editorial staff of the MEDICAL ANNALS wishes many years for well earned gentler pursuits.

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# Health Dept. Notes

### Premarital Blood Tests

A CONGRESSIONAL ACT requires applicants for a D. C. marriage license to have a serological examination. Public Law 89-682 became effective on January 15, 1967. It forbids the D. C. Marriage Bureau to accept a marriage license application unless the persons applying have submitted to a standard laboratory blood test within 30 days prior to the date of application.

The legislation provides opportunities to find unknown cases of infectious syphilis and encourage positive reactors to seek medical care.

A Premarital Blood Examination Form (PH 543-22), prescribed by the Board of Commissioners of the District of Columbia, must be signed by a physician licensed to practice medicine or osteopathy in D. C., a commissioned medical officer in the military service or U. S. Public Health Service, or a person in D. C. certified by the Department of Public Health as duly qualified to administer and interpret a standard laboratory blood test. The form must certify that the applicant does not have syphilis in a communicable stage and must accompany each application for a marriage license.

Copies of the form may be secured from the D. C. Medical Society, D. C. Marriage Bureau, private laboratories, and the Venereal Disease Control Division and Bureau of Laboratories of the D. C. Department of Public Health.

Blood tests performed in states or territories other than the District of Columbia will be accepted provided that sufficient information is furnished and the laboratory performing the test is approved by the state or territory. Persons filing such laboratory forms are referred to the Bureau of Laboratories or the Venereal Disease Control Division of the D. C. Department of Public Health. If the serological test is acceptable to the Department, Form PH 543-22 will be issued. The Health Department has received a number of requests from servicemen with the Armed Services in England, France, Korea, Germany and Vietnam.

Blood may be drawn by a private physician and tested in the Health Department's Laboratory located in the Municipal Center or in an approved private laboratory. Twenty-eight private laboratories in D. C. are approved to make the serological tests. If the test is negative, Form PH 543-22 is completed by the physician. Individuals with a positive serology will be contacted by a Health Department representative to locate the source of infection.

A Judge of the U. S. District Court for the District of Columbia may waive the requirement of a serological test before marriage.

The law directs the D. C. Department of Public Health to conduct serological tests without charge for persons unable to pay for the services of a private physician. Three Department clinics make these tests available: Northwest Central Clinic, 1325 Upshur Street, N.W., Southwest Health Center, 850 Delaware Avenue, S.W., and D. C. General Hospital, 19th and Massachusetts Avenue, S.E.

During the first quarter of this year, 3,268 blood tests were taken. Of this number, 2,258 samples were tested in the Health Department laboratory, and 1,010 samples were tested in approved private laboratories. During the same period 1,609 applications for marriage licenses were filed, compared with 2,267 applications in the first 3 months of 1966. Twenty-five couples who had taken the premarital examination allowed the 30-day period to lapse. Should any of them again decide to file an application for marriage license, another blood test must be made.

MURRAY GRANT, M.D., D.P.H.
*D. C. Director of Public Health*

# Report of the Delegates to the AMA House of Delegates

## Atlantic City, N. J., June 18–22, 1967

The Annual Session of the House of Delegates was faced with the largest number of resolutions and reports ever presented. While a number of the actions taken reflected the desire of the AMA membership to minimize the impact of governmental influence on the conduct of programs financed in whole or in part by Federal funds, there were specific actions of other types which are called to the attention of this Society.

1. The report of the Committee on Human Reproduction, chaired by your senior delegate, Dr. Raymond L. Holden, was approved by the House of Delegates with only minor editorial changes. It is the first policy statement of the AMA since 1871 on therapeutic abortion. While the entire report is available it may be summarized by saying that the AMA recognizes that there are many physicians who on moral or religious grounds oppose therapeutic abortion under any circumstances, and the AMA is opposed to induced abortion except when there is documented medical evidence that (a) the health of the mother is in danger, (b) continuation of pregnancy resulting from legally established statutory or forcible rape or incest may threaten her health, or (c) the infant may be born with incapacitating physical deformity or mental deficiency. Two requirements were adopted in the report which then permit a physician "to prescribe and administer treatment commensurate with sound medical judgement and currently established scientific knowledge": (1) that 2 other competent physicians examine the patient and concur in writing, and (2) that the procedure be performed in a hospital accredited by the Joint Commission on Accreditation of Hospitals.

2. A resolution from this Society requesting a study of Federal Health Programs in order to eliminate or reduce duplication, and hence waste of money, was referred to the Board of Trustees.

3. Another resolution from this Society asking consideration of regional rather than national conferences in order to reach the membership at large was adopted and referred to the Board of Trustees.

4. Long hearings were held regarding the AMA Group Disability Insurance Program. In essence, the Reference Committee recommended, and the House of Delegates directed the Board of Trustees to attempt to continue the same premium-benefit structure as now exists with adequate safeguards for the members and the program.

5. The House of Delegates made known its disapproval of the use of the name "American Board" in the title of any unapproved Board, thereby misleading the public and the profession. This refers to any "Board" in any medical specialty.

6. Any action on the Millis Report on Graduate Medical Education was deferred until June 1968.

Raymond T. Holden, M.D.
C. Willard Camalier, Jr., M.D.
*Delegates*

# Dr. Wilbur to Head AMA in 1968

Dr. Dwight L. Wilbur, of San Francisco, was elected President-elect of the American Medical Association, June 21, during its 116th Annual Convention in Atlantic City, June 18–22. Dr. Malcom E. Phelps, of El Reno, Oklahoma, was elected Vice President. Dr. Wilbur has served as a member of the Board of Trustees of the AMA since 1963. The son of a former President of the AMA, Dr. Ray Lyman Wilbur, he has been on the Clinical Faculty of Stanford University School of Medicine for 30 years and since 1949 as Clinical Professor of Medicine. He will assume the presidency in San Francisco in June 1968.

Dr. Milford O. Rouse, of Dallas, Texas, was installed as President of the AMA, June 20, in special ceremonies in the Pennsylvania Room at Haddon Hall. The 122nd President, he succeeded Dr. Charles L. Hudson, of Cleveland, Ohio.

The Distinguished Service Award went to Dr. E. W. Alton Ochsner, of New Orleans, surgeon and Professor Emeritus of Surgery at Tulane University School of Medicine. Gregory Pincus, Sc.D., Research Director of Worcester Foundation for Experimental Biology, Shrewsbury, Mass., received the Scientific Achievement Award for his pioneer research in oral contraceptives. This award is bestowed upon a nonphysician scientist for outstanding work in his field.

Dr. Irvine H. Page, of Cleveland, Ohio, was selected as the 1967 Passano Foundation Laureate. Past President of the American Heart Association, Dr. Page received the $5,000 award for his outstanding contributions to the understanding of the pathogenesis and pathophysiology of hypertension.

A team of Washington physicians received Honorable Mention in the Scientific Exhibit of the Section on Dermatology. They were: Drs. Teoman Saracli, Robert L. Baird, Thomas E. Reichelderfer, Roland B. Scott, Angella D. Ferguson, and John A. Kenney, Jr., of Howard University College of Medicine, Freedmen's Hospital and District of Columbia General Hospital; their exhibit was entitled, "Pediatric Dermatology (Observations on Negro Infants and Children)."

Dr. Fred A. J. Geier, of Washington, was one of 32 physicians honored at a special luncheon for AMA Volunteer Physicians for Vietnam who had served a minimum of 90 days in Vietnam.

Mrs. Karl F. Ritter, of Lima, Ohio, was installed President of the Woman's Auxiliary to the AMA at the Shelburne Hotel, June 21, succeeding Mrs. Asher Yaguda, of Newark, N. J.

Mr. George B. Larson, retiring Director of the Convention Services Department, was honored at a reception and dinner, June 20, at the Smithville Inn, near Atlantic City.

# DOCPAC Briefs

or

## The Political Left Takes No Vacation

We are now in the midseason lull as far as national politics are concerned. There is some talk about presidential candidates and primaries, but people at the moment are pretty uninterested in politics. However, have you stopped to think that our political enemies are not resting. They are out actively working and registering people now for the campaign ahead, a year from this coming November. They are planning and financing and working hard.

What are you doing, Doctor? Join DOCPAC now and help in every congressional race throughout the United States. We must not be complacent. The present status of American medicine is threatened constantly by selfish interests from the left. Help shape the future of America, both political and medical, by joining your District of Columbia Political Action Committee.

William H. Cooper, M.D.
*Chairman, D. C. Political Action Committee*

## Drug Dependence, Addiction, Habituation

Writing in the *Bulletin of the World Health Organization*, Eddy et al[1] sought to substitute the concept of drug dependence, classified by the type of agent involved, for the confusing and unsound terms "addiction" and "habituation." The authors emphasized that dependence may be psychic, physical, or both, and that tolerance may or may not be present. Their classification, now gaining general acceptance, includes the following types: morphine, barbiturate-alcohol, cocaine, marijuana, amphetamine, khat, and hallucinogen (LSD).

Committee on Problems of Drug Dependence
*Washington Psychiatric Society*

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[1] Eddy, N. B., and others: Drug dependence: its significance and characteristics. Bull. WHO, 1965, 32, 721.

N.B. The Committee would appreciate it if members of the D. C. Medical Society will comment on or relate their experiences concerning problems of drug abuse or misuse.

## Patients Needed at Clinical Center

The coöperation of physicians is requested in a continuing clinical study of Waldenström's macroglobulinemia and related hyperviscosity syndromes being conducted by the National Cancer Institute at the Clinical Center.

Of interest are patients with retinopathy, mucous membrane bleeding, vertigo, or other clinical disorders associated with elevated serum viscosity. Patients should be willing to participate in studies which will include a thorough evaluation of clinical status and measurement of pulmonary and cardiac blood flow before and after reduction of serum viscosity by plasmapheresis. Anticipated hospitalization is about 3 weeks. Upon completion of their studies patients will be returned to the care of the referring physician, who will receive a full report of the studies done.

Physicians may write or phone one of the following: Drs. John R. Wunderlich, Dean L. Mann, or John L. Fahey, Clinical Center, Room 4B-18, National Institutes of Health, Bethesda, Md. 20014; telephone: 656-4000, Ext. 65461.

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The long-continued action of Novahistine LP should help you both get a good night's sleep. Two tablets in the morning and two in the evening will usually provide round-the-clock relief by helping clear congested air passages for freer breathing. Novahistine LP also helps restore normal mucus secretion and ciliary activity—normal physiologic defenses against infection of the respiratory tract. Use cautiously in individuals with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Caution ambulatory patients that drowsiness may result. Each Novahistine LP tablet contains: phenylephrine hydrochloride, 25 mg., and chlorpheniramine maleate, 4 mg.

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# Photocopying—A Threat to Scientific Publishing*

**Statement of William M. Passano for the Williams & Wilkins Company, of Baltimore, Maryland, on S.597 for the General Revision of the U S. Copyright Law before the Subcommittee on Patents, Trademarks, and Copyrights Committee on the Judiciary, U. S. Senate, April 12, 1967.**

My name is William M. Passano, and I will be joined later in our testimony by Mr. Lyle Lodwick. I am President of The Williams & Wilkins Company and Director of Waverly Press, Inc., a jointly-owned and affiliated company. We are publishers and printers of scientific journals and books, have over 800 employees in Baltimore and Easton, Maryland, and are in our 76th year of operation.

While our business is not small, our markets for our products are very small—so small, in fact, that the loss of 2 or 3 sales for some of our books and journals in each of the few hundred major markets for our products around the world can make their publication unprofitable.

We have 4 compelling reasons for wishing to testify before this Committee. The first is that we are a major publisher of scientific periodicals, which are particularly vulnerable to piracy by photocopying, and there has been little testimony on this subject.

The second reason is that we wish to concentrate attention on the threat from photocopying rather than the threat from the computer. It is true that the computer may prove to be in the near future a real threat to owners of copyrighted material, but the threat from photocopying is with us now. It is a known, tangible matter and could and should be dealt with now, before it is too late.

Our third reason is that we are not in a position which requires that we pull our punches for fear of offending our good customers. It is true that most of our customers are in education, but they are in higher education. The great majority of those we have talked with are of the opinion that uncontrolled photocopying—for all of its immediate advantages to the educator—poses a most serious and immediate threat to scientific publishing, and therefore, to the scientific world in general.

Our last reason is that we are an independent publishing house in no way owned by or connected with a manufacturer of computers, copying machines, or any other electronic devices. Therefore, what we have to say need in no way be diluted by the necessity of "listening to his master's voice."

Let me deal with the threat of "photocopying" to the average scientific periodical. We know that photocopying has already seriously reduced the income of most of the 39 periodicals which we publish. (Incidentally, of this number 25 are published by us for scientific societies and 14 are owned by my company outright.)

It is easy to visualize how this erosion of income takes place. An individual scientist, instead of subscribing to a journal in his field, will go to a library and look over the table of contents of the most recent issue and get photocopies of those articles which interest him or which he would like to file away for future reference.

The research laboratory or other institution, instead of subscribing to several copies of the periodical appropriate to its work, will subscribe to 1 copy and make photocopies of it to distribute among the persons working in the laboratory.

A research worker wanting to collect copies of articles which apply to his particular research project, rather than writing the authors of these articles and asking them to supply reprints, which we as publishers have previously supplied to the authors, will photocopy the articles in question instead.

An individual or institution, instead of purchasing from us back numbers or back volumes of a periodical which have appeared prior to the current subscription to it, will go to the library and make photocopies of those articles or perhaps even of complete issues which are his special interest.

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* Editor's note: The subject of photocopying and copyright may seem of little concern to the medical profession. However, the impact of the proposed revisions of the U. S. Copyright Law poses a threat to scientific publishing which could eventually curtail drastically the dissemination of scientific information through privately owned publishing houses as well as journals published by non-Government organizations and institutions. This testimony states the case for private publishers from the viewpoint of Mr. Passano, Director of Waverly Press, which has printed the Medical Annals since its inception in 1932.

The statement of Mr. Lodwick which follows his testimony is a very brief condensation of a plan for setting up a formula which he believes would give a fair and equitable monetary return to owners of copyrighted material.

You may ask, how do we know that this takes place?

In the first place, we have talked to librarians and scientists all around the country and they tell us that it does, in fact, take place and in great quantities. Some of our periodicals are photocopied more violently than others, but none escape.

In the second place, the growth of our subscription business in these boom times of the 1960's lagged behind the growth of the market. It seems to us that the handwriting on the wall is obvious.

Three years ago we started 4 new periodicals. Before doing so we were very confident that the editorial content of these periodicals was excellent and filled a long-felt need. Of course, we expected these new journals to lose money at the start, but they not only did this but are continuing to lose money today when they should, by all rights, have been on a self-supporting basis. We have been told that these journals are in considerable demand for photocopying.

It seems obvious to us that the failure of their subscription lists to grow to a point where they would be self-supporting is due to the fact that persons who otherwise would subscribe are depending on photocopying to supply their needs.

We as a medical publisher are not the only loser in this situation. The profit shown by the 25 periodicals that we publish for scientific societies is shared with the societies. As uncontrolled photocopying reduces the income of these periodicals, the society's income is reduced as well as our own. When the circulation is curtailed to the point that income fails to cover expenses, then of course the periodicals either go out of existence or must be kept alive by government subsidy.

This photocopying is illegal under the present copyright law and would be equally illegal under the new copyright law. The difficulty is that the term "fair use" salves the conscience of anyone who wants to make a copy of an article appearing in one of our journals. It is a little bit like the use of alcoholic beverages in Prohibition days. A man who wanted to take a drink was going to do so regardless of what the law said in the matter, and the man who wants to make a photocopy is going to do so as long as nobody is looking over his shoulder to tell him no.

It is unrealistic to think otherwise and to believe that examples of what might be considered "fair use" in the House report are in any way going to cut down on the billions of photocopies which are made annually today of copyrighted material.

In our opinion, there are only 2 roads to follow if there is a serious intention to protect the rights of the copyright owner against the economic competition of the copying machine. One is to ban the use of photocopying machines unless they are operated by institutions who are charged with the responsibility of seeing that no copyrighted material is copied without the permission of the copyright owner.

We feel that it is unrealistic and not in the public interest to consider restricting in any way the use of photocopying devices. They serve a very useful purpose in the dissemination of knowledge. Since we, as publishers, are in that business, we certainly don't want to see the spread of knowledge curtailed.

To us, the only solution to the problem is a simple system of royalty payments with a minimum of red tape. At this point I want to turn the floor over to Mr. Lyle Lodwick, Director of Marketing of my organization, who will explain to you how and why we arrived at this conclusion and how such a system will work in actual practice.

### Summary of Testimony by Mr. Lodwick

The Williams & Wilkins proposal calls for a small tax on all copying machines to set up a copying-royalty clearing house and to fund periodic distribution of copying-royalties to copyright owners. Copyright owners would receive per-page royalties in direct proportion to the number of pages photocopied nationally.

The basis for determining accumulated royalty payments would be from a national sample determined by libraries, which would report to the clearing house the number of pages copied from each source having a copyright notice in their holdings. The distribution formula would be applied to all other copying of copyrighted works.

The advantages claimed for this proposal are: no red tape to users, who neither have to request advance permission nor report copying and pay royalties directly to the copyright owners; low "collection costs"—in effect, a hidden tax collected by the copying machine manufacturer or other owner of the machine; provides income necessary to operate scientific journals faced with losses of subscriptions, back volume, and reprint income due to "convenience copying" by potential customers.

(*Continued on page 498*)

# Question of the Month—?

"Medical meetings are literally coming out of the doctors' ears" is a fair statement. This seems to be the result of competition between medical schools, hospitals, specialty societies, voluntary health agencies, drug companies, and the private medical societies. **Since doctors who are the basic catalysts of this competition decry the whole trend, can we get a meeting of minds to develop sensible coördination and unity to reduce the number of meetings?**

## Answers and Comments

JOHN C. ROSE, M.D. (Medical Education): I deny that the situation is excessive, that it results from "competition," or that all doctors "decry" the trend.

Washington is a sophisticated medical community. Every day there are learning opportunities for practicing physicians of every specialty, at different hours and at various places. This is good. No one is forced to attend. There's a good selection from which to choose.

We've all heard the distant rumblings about reëxamination and periodic relicensing of physicians in the future. It can happen. The profession must establish a recognized continuing educational system that works and in which every physician participates.

With all of the meetings that are available, as the question implies, it would be a revelation to know how many physicians go to no educational meetings. Could it be 25 per cent of the licensed physicians of Washington? More?

The public knows that a physician can quickly become obsolete and that his career is one of "lifetime learning." The public now even knows about the role of the drug company contact man. It would be good for us to seize the initiative for once and show the public the extensive continuing educational program that exists for the physicians of Metropolitan Washington. Let our patients know that every week there are numerous opportunities for each physician to keep abreast of developments in his field. It will be a great day when we can demonstrate that all physicians are doing it.

W. MONTAGUE COBB, M.D. (Medical Education): In addition to the competition for the physician's time from meetings, there is also the deluge of literature from the throw-away periodicals. I do not think organized effort will reduce the number of meetings or advertising media. Each doctor must decide for himself which meetings he can ill afford to miss and which medical journals he will cover regularly.

CALVIN T. KLOPP, M.D. (Surgery): There are 2 parts to this problem—national or international meetings and local meetings. Each must be dealt with separately.

National meetings take care of themselves. If programs are not sufficiently good, attendance dwindles, and eventually the poorly attended meeting is no longer held. Therefore I see no problem with national meetings.

Local meetings are generally always poorly attended unless of excellent quality. To make up for this, many such meetings become primarily social affairs and should be so considered. All others might well be required to have prior approval of the local Medical Society, which should limit the number and increase the quality of each. Individual hospital programs should be discouraged, as should small society meetings, in favor of community-wide, coördinated, coöperative, excellent programs.

**If any members have dissenting views, your Editorial Staff will be pleased to receive and publish them.**

# A sharp needle just burst her fairy-tale bubble

**Why did he hurt me, Mommy?**

Her "feelings" are more hurt than her finger. She was excited about the special visit to the doctor . . . he's an old friend. Now suddenly here's this very unfriendly business with a quick-jab of a needle that made her finger bleed! She doesn't understand that this laboratory test will help the doctor protect her blooming good health. She's lucky. Before 1900, as many as one-fourth of all babies born died before they were a year old. Today's statistics show that she'll probably enjoy at least 75 years of wonderful living. One day she'll be soothing the "hurt feelings" of her own little girl, or even a little grand-daughter, who will then be protected by even greater achievements in medical science.

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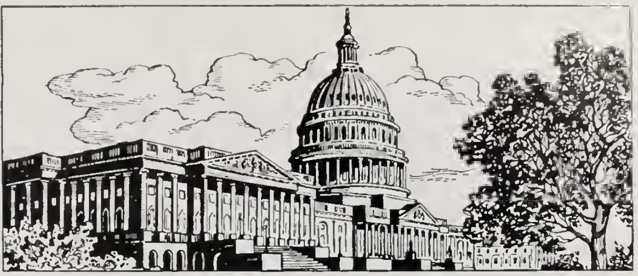

# NEWS & PERSONALS

## Summary of Executive Board Actions

### Proceedings of June 5 Meeting

Dinner for the Board Members was served at 6:40 p.m. in the Exhibit Hall of the Medical Society. Dr. Karl C. Corley, Chairman, presided at the meeting. Present were Drs. Frank S. Bacon, C. Willard Camalier, Jr., Henry D. Ecker, Raymond T. Holden, Margaret M. Kenrick, William S. McCune, Edward W. Nicklas, Paul R. Wilner, and Mr. George W. Cooley, Secretary. The meeting was called to order at 7:20 p.m.

The minutes of the April 24, 1967 meeting were approved.

**Committee Meetings:** The Secretary reported the following committees had met since the last regular meeting of the Board:

| | | |
|---|---|---|
| April | 24 | Ad Hoc Committee on Medical Licensure |
| | 26 | Committee on Regional Medical Programs |
| | 27 | Committee on Communicable Diseases |
| | 27 | Ad Hoc Committee on Liaison with the Clergy |
| | 28 | Medical Bureau Subcommittee |
| May | 4 | Committee on Regional Medical Programs |
| | 5 | Ad Hoc Committee on Multiphasic Screening |
| | 5 | Subcommittee on Liaison with the D. C. Bar Association |
| | 10 | Representatives of Office of Dependents' Medical Care |
| | 10 | Advisory Group to Regional Medical Programs |
| | 11 | Conference with Food and Drug Administration |
| | 15 | Executive Board Policy Meeting |
| | 16 | Insurance Committee |
| | 16 | Grievance Committee |
| | 17 | Board of Credentials |
| | 19 | Committee on Child Welfare |
| | 22 | Committee on Constitution and By-laws |
| | 22 | Committee on Occupational Health |
| | 23 | Insurance Committee |
| | 23 | Membership Committee |
| | 23 | Committee on Liaison with the Clergy |
| | 24 | Public Welfare Committee |
| | 29 | School Health Coördinating Committee |

**Board of Credentials:** The following actions were taken on recommendations made by the Board of Credentials:

*Active Members*

Theodore R. George, Jr., 229 Jefferson Street, N.W.
William Lionel Matzkin, 4000 Albemarle Street, N.W.
Harold Margulies, 1501 New Hampshire Avenue, N.W.
Panagiotis Pappous, 1801 Eye Street, N.W.
Donald Joseph Sewell, 6209 14th Street, N.W.
Don S. Wenger, Andrews Air Force Base

*Associate Members*

Arnold G. Brody, 6700 Belcrest Road, Hyattsville, Md.
Gary D. London, U. S. Public Health Service

*Transfers*

*Active to Associate:* George J. Ellis, Jr., and Juan G. Machado
*Active to Special:* Reuben Goodman
*Associate to Life:* John L. DeMayo
*Associate to Active:* Rafael A. Borgos, Miguel A. Cano, Ranville S. Clark, Robert L. Flynn, Z. Efrain Guerrero, Mohammad F. Talegani, Alkinoos Vourlekis, Edith H. Weigert, and Wai Tuen Wong.
*Resident-Intern to Active:* Robert T. Greenfield, Jr., Michael Anthony Jackson, and Marianne I. Schuelein.
*Associate to Resident-Intern:* Vincent P. Sweeney

*Reinstatements*

*Active:* William Beaven, Andrew F. Burton, Frank J. Grabill, and Margaret E. Grigsby.

*Resignations*

*Active:* A. Beryl Farfel, Charles E. Higbee, and Ludwig G. Lederer

**Ad Hoc Committee on Multiphasic Screening Program:** President Ecker had appointed this Committee, at the request of the Executive Board, to review the first 3 years of the Multiphasic Screening Program of the D. C. Health Department. A copy of the report of this Committee had been sent to each member of the Board. After considerable discussion, in which there was some criticism of the reports sent to physicians by the Health Department, the following action was taken: That the recommendation of the Ad Hoc Committee on Multiphasic Screening be approved, with the further recommendation that the Health Department be notified that the reports which are sent to physicians are frequently not clear and should be revised.

In taking this action, the Board endorsed the continuation of the Multiphasic Screening Program of the D. C. Health Department, including the proposed unit at D. C. General Hospital, the possible addition of new test procedures, and a recommendation to the Health Department that any announcements of this Program to new groups specify that no individual should consider these screening tests as a substitute for a visit to his or her physician, since screening is never a substitute for a physical examination.

**Membership Committee:** The report of this Committee contained recommendations which would constitute a general charge to the Committee and which would be undertaken over a period of time. These recommendations, which were approved by the Board, concerned inviting new physicians coming to the District of Columbia and members of the medical school and hospital staffs, not now members, to become members of the Society; a brochure on the Society's activities; a membership roster; annual program for senior house officers to inform them of problems on entering practice; and letters of sympathy and offers of assistance to families of deceased members.

**Committee on Communicable Diseases:** The Secretary referred to a 1-page summary report from this Committee which recommended that the Board consider a follow-up of the Measles Vaccine Program undertaken in March by the Health Department, with the support of the Medical Society. At that time parents were urged to have their children obtain the measles vaccine in physicians' offices. The follow-up would be a city-wide program similar to the Polio Immunization Program, involving 30 to 40 sites. In view of the fact that this program would cost the Society at least $27,000, and perhaps more, the matter was referred back to the Committee to consider possible sources of funds for financing this program.

**Committee on Child Welfare:** The Committee requested the Board to make certain recommendations to area hospitals in reference to the obstetrical services and the privileges of pediatricians in these hospitals. It was agreed that this was a matter that should be considered by the Committee on Liaison with Medical Schools and Hospitals.

**Committee on Medicolegal Problems:** The first request from this Committee was that the Board accept in principle the reactivation of a Case Review Committee after further investigation and consideration by the Medicolegal Committee. In this request the Board acquiesced.

The second recommendation was that this Case Review Committee be made a permanent Subcommittee of the Medicolegal Committee. No action was considered necessary at this time.

The third item in the report concerned a request from the Dental Society for aid in establishing a similar committee for its Society. Dr. Ecker pointed out that this would entail permitting representatives from the Dental Society to sit in on some meetings or some portions of meetings of the Medicolegal Committee to see how the Committee operates. It was agreed that the Dental Society should be offered such assistance.

**Pilot Medical Communications Project:** Prior to this meeting, at the request of Dr. Nicklas, the Secretary had sent members of the Board copies of 2 news items regarding the availability of Federal funds for the transmission of medical information to physicians via local television. The first such educational program had been established in Atlanta, Georgia, and Dr. Nicklas thought the Board might give consideration to a similar program in the District of Columbia. It was voted to refer this matter to the Committee on Postgraduate Education, with the suggestion that it keep in mind the program now being undertaken in reference to P.L. 89-239, and to report back to the Board at its earliest convenience.

**Occupational Health Committee:** The Occupational Health Committee has now agreed to consider the new Relative Value Scale of the Medical Society of the District of Columbia as a basis for developing a new schedule of fees for Workmen's Compensation cases. The local District Claims Managers' Association has withdrawn from participation in this project and therefore any new fee schedule will be a unilateral schedule prepared by the Society.

**Committee on Constitution and By-Laws:** The first item in the report of this Committee had to do with the number of requests received by the Board of Credentials from Associate members who wish to become "Life" or "Special" members. The Committee on Constitution and By-laws does not believe that the present By-laws of the Society should be changed to permit other than Active members to become "Life" or "Special" members, and that where such requests are received by the Board of Credentials they should be referred to the Executive Board, which has the authority to remit dues in full or in part, and temporarily or permanently. The Board approved this method of handling such requests.

The second item concerned a revision of Chapter II, Article V, which deals with Associate members. The Committee recommends that in line 11 of Article V the following be inserted before the word Sections: "be members of," and the following be inserted after the first use in line 11 of the word Society: "where they may vote and hold office as provided in Chapter X." The recommendations of the Committee in regard to Associate members were approved.

The final item in the report of the Committee related to the fact that there is no authority in the Constitution and By-laws for the Executive Board to employ an Executive Director and that the Committee is considering an amendment which might provide for this.

### Progress Reports

President Ecker and the Secretary reported that an agreement had been reached with Dr. Murray Grant on legislation to amend the Healing Arts Practice Act.

The Secretary reported on 3 additional matters:

1. That the Section on Ophthalmology had submitted recommendations relative to the proposed legislation on optometry in the District of Columbia.

2. The status of the renewal of the ODMC contract for 1967–68. Three Medical Societies in Virginia had voted not to participate and therefore would not be parties to a revision of the old contract. At present Prince George's County is the only County Society which has agreed to participate in a renewal of the ODMC contract but a decision is expected from Montgomery County Medical Society within the next week. Following this, General Peatfield will be notified of the situation and it will be up to him to decide whether the nearby Virginia counties will be serviced by Medical Service of D. C. or should return to the program of the Virginia State Medical Society. Maryland has no contract and Maryland Blue Shield administers the program for ODMC.

**FORSTER PORTRAIT UNVEILED: A portrait of Dr. Francis M. Forster, formerly Dean of Georgetown University School of Medicine, was recently unveiled during a ceremony at the University's Medical Center. Shown with the portrait are (left to right): Dr. Forster, who is now Chairman of the Department of Neurology at the University of Wisconsin; Dr. Desmond O'Doherty, Chairman of the Department of Neurology at Georgetown; the Reverend Mark H. Bauer, S.J., Vice President for Medical Affairs at the University; and Dr. John C. Rose, Dean of Medicine at Georgetown. The portrait, which hangs in the Medical-Dental Building, was painted by Mary Lois Egeli Ekroos, of Valley Lee, Md., daughter of Bjorn Egeli, well-known portrait artist.**

3. Dr. William P. Herbst had suggested that the Board consider selecting the Kober Lecturer for 1968. It was agreed that this matter should be referred to the Committee on Postgraduate Education.

The Secretary asked whether the Society had any policy in reference to members accepting referrals from osteopaths. It was agreed that the Society had no such policy and therefore any referrals of this type were acceptable.

Dr. Holden reported on his meeting with representatives of the Red Cross Blood Bank. He pointed out that a number of questions had been raised in reference to liaison between the Society's Committee on Blood Banks and the Red Cross, and he reviewed some of these problems in detail. He also read a statement, "Use of Packed Red Blood Cells," prepared by Dr. Jack J. Rheingold, which he thought should be inserted in the Medical Annals (see page 479).

A motion was made and carried that the Committee on Blood Banks meet with Dr. Holden and Dr. Van der Aue to discuss the use of fractionated blood cells and to improve coöperation between the Committee and the Red Cross.

The original articles of agreement between the

Red Cross and the Medical Society were reviewed briefly and it was agreed that the Committee on Blood Banks should have more physicians who would be called "users of blood." Dr. McCune, President-elect, and President Ecker consented to review the agreement and discuss its status with Dr. Holden.

There being no further business, the meeting adjourned at 10:30 p.m.

## General News

WRC-TV, in cöoperation with the U. S. Department of Health, Education, and Welfare and St. Elizabeths Hospital, has produced a 10-part **educational TV color series entitled "The Disabled Mind."** It will be shown weekdays from 6:30 to 7:00 a.m., August 28 through September 8, on Channel 4.

The program will show actual patients in states of various therapies and their responses to professional staff members and trainees at St. Elizabeths Hospital in Washington, D. C. Producer-director Richard Cox spent a year in research at St. Elizabeths and selected 100 patients who represent many of the problems found among the mentally disabled. The patients were brought to the WRC-TV studios for filming, and the therapeutic sessions were reconstructed to duplicate the original sessions as nearly as possible. Moderator-host of the series will be Dr. Francis N. Waldrop, Director of Training and Behavioral Studies at St. Elizabeths.

**Individual membership in the World Medical Association** was opened for the first time to physicians following the 20th World Medical Assembly, held last winter in Manila. Associate membership is now available to all members of the 60 national medical associations which comprise the WMA, including the American Medical Association.

Dues are $10 per year, which includes a subscription to the *World Medical Journal* and the privilege of participation in the World Medical Assembly each year. The 21st Assembly will be held in Madrid, Spain, September 10–17, 1967; the 1968 Assembly will be held in Australia.

Application for individual membership should be accompanied by a check for $10, payable to The World Medical Association, Inc., and sent to the Headquarters Secretariat at 10 Columbus Circle, New York, N. Y. 10019.

**The Audio-Digest Foundation** (a nonprofit subsidiary of the California Medical Association) has just released its **1967 Catalog of Classics,** which lists more than 300 1-hour tape recordings devoted to comprehensive panel discussions and symposia on everyday office problems. These tape recordings, available to individual physicians, hospitals, and clinics, cover material in 7 specialty areas: anesthesiology, obstetrics-gynecology, surgery, pediatrics, internal medicine, ophthalmology, and general practice. A number of tapes also focus on cancer, psychiatry, gastroenterology, cardiology, arthritis, geriatrics, and hematology.

The recordings represent distillates of on-the-spot recordings from several hundred major meetings of such groups as the American Medical Association, American College of Physicians, American Society of Anesthesiologists, American College of Obstetricians and Gynecologists, as well as condensations of major university postgraduate courses.

The Catalog of Classics is available free of charge and may be obtained by writing the Audio-Digest Foundation, 619 South Westlake Avenue, Los Angeles, Calif. 90057.

**The first Vivian Gill Chair of Epidemiology and Environmental Health** has been established at **George Washington University School of Medicine** through an initial grant of more than $400,000 from Mr. Tom Gill in memory of his wife. Dr. Jack W. Millar, who heads the new Department of Epidemiology and Environmental Health at George Washington, will be the first to assume the Vivian Gill Professorship. Mr. Gill is an international advisor on worldwide problems of conservation. The long association of the Gills with their friend and physician, Dr. Walter A. Bloedorn, formerly Dean of Medicine at George Washington University, influenced their concern for medical training and assistance.

**Dr. George H. C. Stobie,** a research analyst, is the first physician appointed to the staff of the new Concentrated Care Center of Georgetown University Hospital, scheduled for completion in 1970. He will be Assistant Medical Director and Assistant Administrator. Dr. Stobie came to Georgetown, July 1, from Henry Ford Hospital in Detroit, where he was Assistant Administrator in charge of medical computer development.

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| Vitamin C (Ascorbic Acid) | 300 mg |
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A native of Ontario, Canada, Dr. Stobie studied engineering physics at the University of Toronto, and later, in 1950, he received a medical degree from McGill University. For 2 years he worked as a research assistant at the Mayo Clinic. In 1961 he was appointed Director of Surgical Research at the Hospital for Sick Children's Research Institute in Toronto. He joined the staff of Henry Ford Hospital in 1964.

At its Annual Meeting, June 29, **the Washington Heart Association** reëlected Dr. Jack Kleh as President for 1967–68. Also reëlected for another year were the other officers: Dr. Charles A. Hufnagel, President-elect; Dr. John M. Evans, Vice President; Dr. John B. Johnson, Secretary; and Mr. John E. Sumter, Jr., Treasurer.

During the afternoon meeting, held in the Exhibit Hall of the D. C. Medical Society, the nomination of 5 new persons and the renomination of 11 persons to the Board of Directors were approved. Among those who were reëlected for an additional 2-year term were Drs. Johnson, Frank A. Finnerty, Jr., Edward D. Freis, W. Proctor Harvey, Lawrence S. Lilienfield, Rashid A. Massumi, and Howard C. Pierpont.

**Watson Davis,** Director Emeritus of Science Service, died, June 27, 1967. When Science Service was organized in 1921 by the late E. W. Scripps, Mr. Davis became managing editor and served in that capacity until 1933, when he was appointed Director. He retired last year.

In 1941 he created a Science Youth Division of Science Service, a part of which is known as Science Clubs of America, popular with science-minded boys and girls in elementary and secondary schools throughout the world. He was one of the originators of the Science Talent Search for the Westinghouse Science Scholarships and of the International Science Fair. In his program, "Adventures in Science," on the CBS network, from 1930 to 1959, he interviewed some 1,300 scientists on the research they were conducting in their laboratories.

He is survived by his wife, Mrs. Marion Shaw Mooney Davis, 3620 Garfield Street, N.W.; a daughter, Mrs. Charlotte Davis Mooers, of Cambridge, Mass.; and a son, Miles Davis, of Baltimore, Md.

Through a long and distinguished career, Mr. Davis is credited with popularizing science and the understanding of science by the general public more than any other individual.

# Personals

**Dr. Naomi M. Kanof,** who has served for nearly 20 years as Editor of the *Journal of Investigative Dermatology*, retired as Editor, July 1. The announcement was made at a dinner held in her honor, June 19, at the Hotel Dennis in Atlantic City, during the 30th Annual Meeting of the Society for Investigative Dermatology, which sponsors the *Journal*. She received a testimonial scroll from her colleagues and, in addition, a gift and congratulatory message from 1,000 young patients at Children's Hospital of D. C., where she is a member of the attending staff. Dr. Kanof is Assistant Clinical Professor of Medicine at Georgetown University School of Medicine and a member of the Editorial Board of the Medical Annals.

Appointed in 1948, she was the Journal's second editor. Her successor is Dr. Richard B. Stoughton, of La Jolla, Calif., who is Director of the Division of Dermatology at Scripps Clinic and formerly head of dermatology and Associate Professor of Medicine at Western Reserve University School of Medicine.

**Dr. Lawrence S. Lilienfield,** Professor of Physiology at Georgetown University School of Medicine, was one of a group of medical educators and officials of the American Medical Association and the U. S. Agency for International Development who met in Chicago, May 24–26, with Dr. Ngo Gia Hy, Dean of the University of Saigon Faculty of Medicine, to consider immediate plans for the further development of the joint U. S.-Vietnamese program for strengthening medical education in South Vietnam. Dr. Norman Hoover, an orthopedic surgeon, currently on the staff of the Mayo Clinic, Rochester, Minn., will succeed retiring field director Dr. Hobart A. Reimann, Professor of Medicine and Preventive Medicine at Hahnemann Medical College, Philadelphia.

**Dr. William B. Walsh,** founder and President of Project HOPE, was awarded an honorary Doctor of Humane Letters degree by Beaver College at Glenside, Pa., June 11. Dr. Walsh, who delivered the commencement address for 149 graduating seniors, was recognized as a "physician, teacher, humanitarian, author, and 'Good Samaritan of the Seas,' who brings help and hope to countless numbers in many lands and who exemplifies America at its best. As founder of Project

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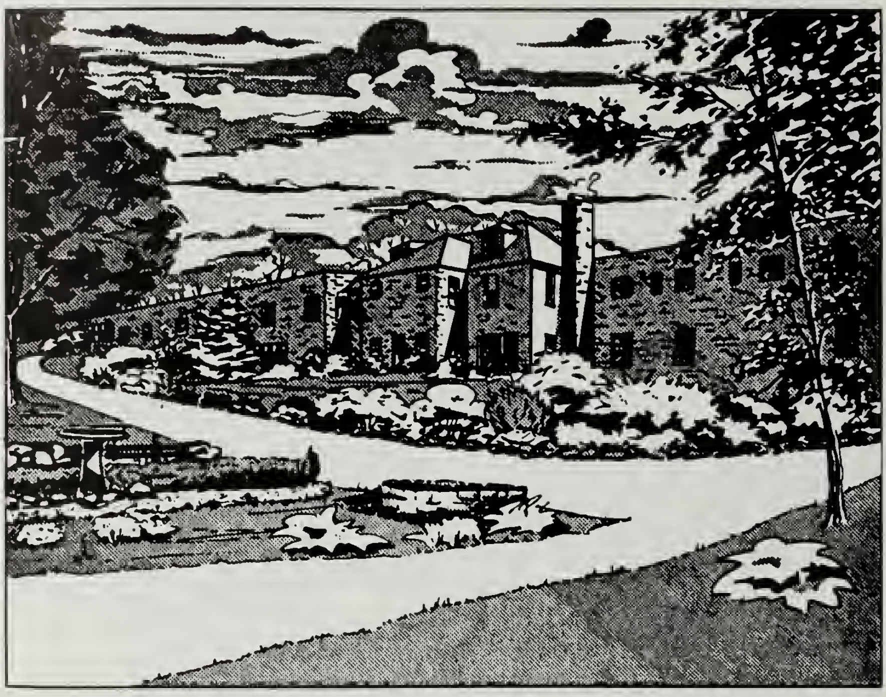

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HOPE, it has been his to achieve what to others might well have remained only a noble idea."

**Dr. Jesse Rubin,** Associate Clinical Professor of Psychiatry at George Washington University School of Medicine, has joined the staff of the new Psychiatric Institute as Director of Outpatient Services. He was Chief of Psychiatric Outpatient Services at George Washington University Hospital before joining the Institute Staff.

Dr. Rubin received his medical degree from Yale University in 1957. After completing his psychiatric residency at Yale University in 1961, he served as Chief Resident of the Yale Psychiatric Institute.

The D. C. Psychiatric Institute, a private psychiatric hospital and treatment center, is a participating member of Group Hospitalization, Inc. Housed on the top floors of the University Medical Building at 2141 K Street, N.W., it opened its facilities the last week in June.

**Dr. Thomas W. Mattingly,** who attended the Annual Meeting of the American College of Physicians in San Francisco, April 10-14, was elected to the Executive Committee of the Board of Governors for a 2-year term. He was also elected Chairman of the Committee on Postgraduate Courses. He is presently serving on its Committee on Military Affairs and Disaster Medical Care.

**Dr. S. Joseph Cosimano,** Washington surgeon, was selected "Sportsman of the Year" by the D. C. Medical-Dental Association Bowling League. The award, a plaque, given for "being a good sport and a team man," and not on the basis of score, was presented to Dr. Cosimano, June 24, at a reception given in his honor.

**GEORGETOWN PEDIATRICIAN OF THE YEAR: Georgetown University bestowed its Pediatrician-of-the-Year Award for 1967 on Dr. Dorothy V. Whipple, Clinical Associate Professor of Pediatrics. The Award is given annually to a pediatrician from the Washington area who has contributed notably to that field during the year. Making the presentation is Dr. Joseph A. Bellanti, Associate Professor of Pediatrics, during a banquet, June 7, at the International Club in Washington. Dr. Whipple authored the book, "Dynamics of Development: Euthenic Pediatrics," which was reviewed in the February 1967 issue of the MEDICAL ANNALS.**

Sibley Hospital Team No. 1 won the competition for the 1966–67 season, with bowlers Drs. Frank Baiers, George Ball, Henry Canton, Vincent O'Donnell, and Robert Fleury. The Providence Hospital Team finished second and Georgetown, third. The League has been headed this year by Dr. Eugene J. McDonald; Dr. Claude Shiflet has served as Vice President and Mr. James Carter as Secretary.

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# Obituaries

## Michael J. McInerney, B.S., M.D.

(1905–1967)

Dr. Michael J. McInerney, well known Washington internist, died unexpectedly, June 2, 1967 at his home, 5010 Millwood Lane, N.W. His offices were located at 916 19th Street, N.W.

Dr. McInerney, a Washingtonian, was born, June 30, 1905. A graduate of Central High School, he received the degrees, Bachelor of Science and Doctor of Medicine, from Georgetown University in 1927 and 1931, respectively. He interned at Georgetown Hospital following his graduation from Medical School and served for a year as resident physician at Gallinger Municipal (now D. C. General) Hospital. In 1937 he enrolled for postgraduate study at Harvard Medical School.

For 34 years Dr. McInerney had practiced in the District of Columbia. He was Chief of Medicine at both Georgetown and Providence Hospitals for many years. For more than 25 years he was Clinical Associate Professor of Medicine at Georgetown University.

Dr. McInerney was elected to Active membership in the Medical Society of the District of Columbia in 1935 and at the time of his death he was Chairman of its Board of Credentials. He was serving on the Board of Directors of the D. C. Society for Crippled Children and was Chairman of its Medical Committee. He was a diplomate of the American Board of Internal Medicine, a Fellow of the American College of Physicians, a member of the American Medical Association, the D. C. Society of Internal Medicine, the Washington Heart Association, the Georgetown Clinical Society, the Georgetown University Medical Alumni Association, and Alpha Omega Alpha fraternity. He also belonged to the Kiwanis Club, the Friendly Sons of St. Patrick, and the Chevy Chase and Columbia Country Clubs.

Surviving him are his wife, Mrs. Margaret Somerville McInerney; a daughter, Margot S., and 3 sons, Michael J. III, Thomas S., and Bryan M., all of the home address. He also leaves 2 brothers, Maurice and Martin McInerney, and 4 sisters, Mary, Margaret, Elizabeth, and Katherine McInerney, all of Washington.

## Edna Gerrish Dyar, B.A., M.D., Ph.D.

(1887–1967)

Dr. Edna G. Dyar, a Life member of the Medical Society of the District of Columbia, died, February 3, 1967, in Phoenix, Arizona.

Dr. Dyar was born in Dover, Minnesota, March 17, 1887, to Louis H. and Etta Gerrish Dyar. She received her undergraduate degree from the University of Wisconsin in 1914, her medical degree from the University of Maryland in 1930, and her doctorate in philosophy from George Washington University in 1923. She interned at Rhode Island State Hospital for Mental Diseases in 1931–32 and continued as a resident physician from 1932 to 1936.

From 1936 to 1942 Dr. Dyar was Assistant Physician on the staff of the Chestnut Lodge Sanitarium. During these same years she trained in psychoanalysis at the Washington-Baltimore Psychoanalytic Institute. She was on the teaching staff of the Washington School of Psychiatry for a number of years.

Dr. Dyar was elected to Associate membership in the Medical Society of the District of Columbia in 1938 and to Active membership in 1948. She became a Life member in 1965. She was a member of the American Medical Association, the American Psychiatric Association, the American Society for Research in Psychosomatic Problems, the American Psychoanalytic Society, and the Washington-Baltimore Psychoanalytic Society.

Due to illness she moved away from the District of Columbia in 1962. She lived in Hollywood, California and later in Phoenix, Arizona. The only known relative is a niece, Mrs. Rosita Cornell Smith, who resides at 943 East Murphy Street, Blythe, Calif. 92225.

### Photocopying Threatens Scientific Publishing—Passano

(*Continued from page 486*)

Unless some form of clearing house is established to indirectly compensate scientific publishers, Williams & Wilkins foresees eventual heavy subsidy and, therefore, complete arbitrary control of scientific publishing by the Government.

They feel their proposal gives the scientific community the advantage of no restrictions on the use of the newer copying technologies without the disadvantage of eventual Government domination and control of the intellectual output and society activities of the scientific community if copyright protection and copying income is denied the scientific publisher.

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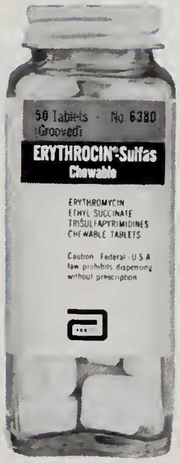
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1. Case Reports on File, Dept. Clin. Development, Abbott Laboratories.
2. Polley, R.F.L., Use of Erythromycin-Sulfas in Office Practice, Western Med., 7:177, July, 1966.

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Brief Summary on next page

**ERYTHROCIN®-SULFAS**
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**Contraindications:** Known sensitivity to erythromycin or sulfonamides. Because of the possibility of kernicterus with sulfonamides, do not use in pregnancy at term, premature or newborn infants.

**Warnings:** As with other forms of sulfonamide therapy, carefully evaluate patients with liver or kidney damage, urinary obstruction, or blood dyscrasia. Deaths have been reported from hypersensitivity reactions and blood dyscrasias following use of sulfonamides. Perform blood counts and liver and kidney function tests if used repeatedly at close intervals or for long periods.

**Precautions, Side Effects:** Occasionally mild abdominal discomfort, nausea or vomiting may occur with erythromycin, generally controlled by reduction of dosage. Mild allergic reactions (such as urticaria and other skin rashes) may occur. Serious allergic reactions have been extremely infrequent. Use sulfonamides with caution in patients with a history of allergy. Assure adequate fluid intake to prevent crystalluria and institute alkali therapy if indicated. If overgrowth of nonsusceptible organisms occurs, withdraw the drug and institute appropriate treatment. If a patient should show signs of hypersensitivity, appropriate countermeasures (e.g. epinephrine, steriods, etc.) should be administered and the drug withdrawn.

**Adverse Reactions:** Sulfonamide therapy may be associated with headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.

Side effects due to erythromycin are infrequent, but occasional abdominal discomfort, nausea, or vomiting, urticaria and other skin rashes may occur.

**Supplied:** The Granules for Oral Suspension come in bottles of 60 ml. and 150 ml. The Chewable tablets are in bottles of 50. Each 5-ml. teaspoonful of reconstituted Granules or each Chewable tablet provides erythromycin ethyl succinate equivalent to 125 mg. of erythromycin activity and 167 mg. of each of sulfadiazine, sulfamerazine and sulfamethazine.

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When you consider using a drug *like* a broad-spectrum antibiotic, why not use a *true* broad-spectrum antibiotic? Like DECLOMYCIN.

References: 1. A.M.A. Council on Drugs: *New Drugs* 1966 ed. Chicago: American Medical Association, p. 12. 2. Osol, A.; Pratt, R., and Altschule, M.D.: *The United States Dispensatory,* 26th ed. Philadelphia: J. B. Lippincott Co., 1967, p. 844. 3. Purcell, R. H., and Chanock, R. M.: Role of Mycoplasmas in Human Respiratory Disease. *Med. Clin. N. Amer.* 51:791 (May) 1967.

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**Warning**—In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, lower than usual doses are indicated, and, if therapy is prolonged, serum level determinations may be advisable. A photodynamic reaction to natural or artificial sunlight has been observed. Small amounts of drug and short exposure may produce an exaggerated sunburn reaction which may range from erythema to severe skin manifestations. In a smaller proportion, photoallergic reactions have been reported. Patients should avoid direct exposure to sunlight and discontinue drug at the first evidence of skin discomfort. Necessary subsequent courses of treatment with tetracyclines should be carefully observed.

**Precautions**—Overgrowth of nonsusceptible organisms may occur. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

**Side Effects**—Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes. A rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose related. Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth — dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs discontinue medication and institute appropriate therapy.

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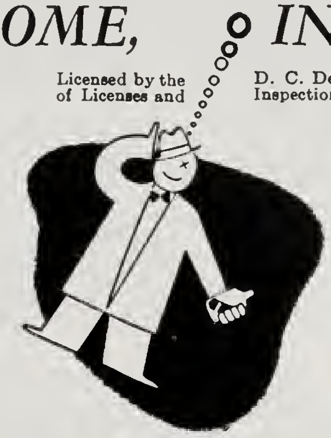

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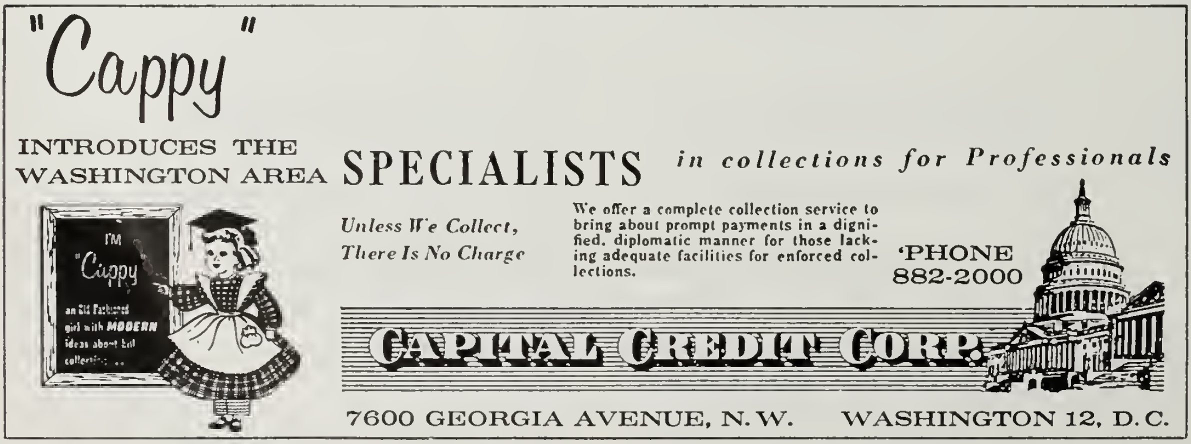
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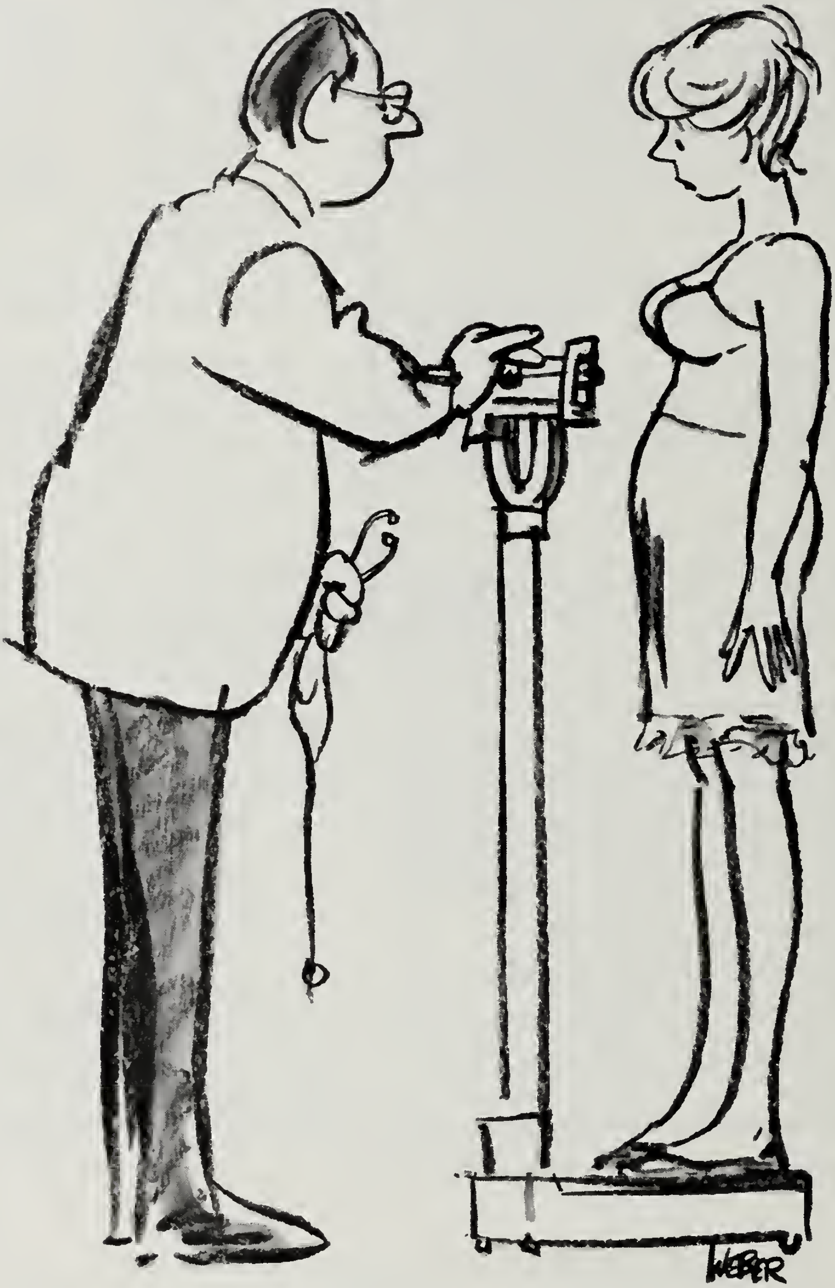

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Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

*Side Effects:* Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness. Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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Tandearil in Painful Shoulder

*Therapeutic Effects:* Stiffness and pain may diminish within 2 days, and full mobility may be restored within a week. These effects are obtained with oxyphenbutazone alone or combined with physiotherapy or local hormonal injections. The drug is usually well tolerated and does not affect pituitary-adrenal function or immune response.

*Contraindications:* Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently.

*Warning:* If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

*Precautions:* Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage. Make regular blood counts. Discontinue the drug and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

*Adverse Reactions:* The most common are nausea, edema and drug rash. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, or a generalized allergic reaction may occur and require withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

*Dosage in Painful Shoulder:* 600 mg. daily in divided doses for 2 to 3 days; 300 mg. daily thereafter. Usual duration of therapy: 2 to 7 days.

*Availability:* Tablets of 100 mg. 6562-VI(B)R

For complete details, please refer to full prescribing information.

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helps painful shoulders move again

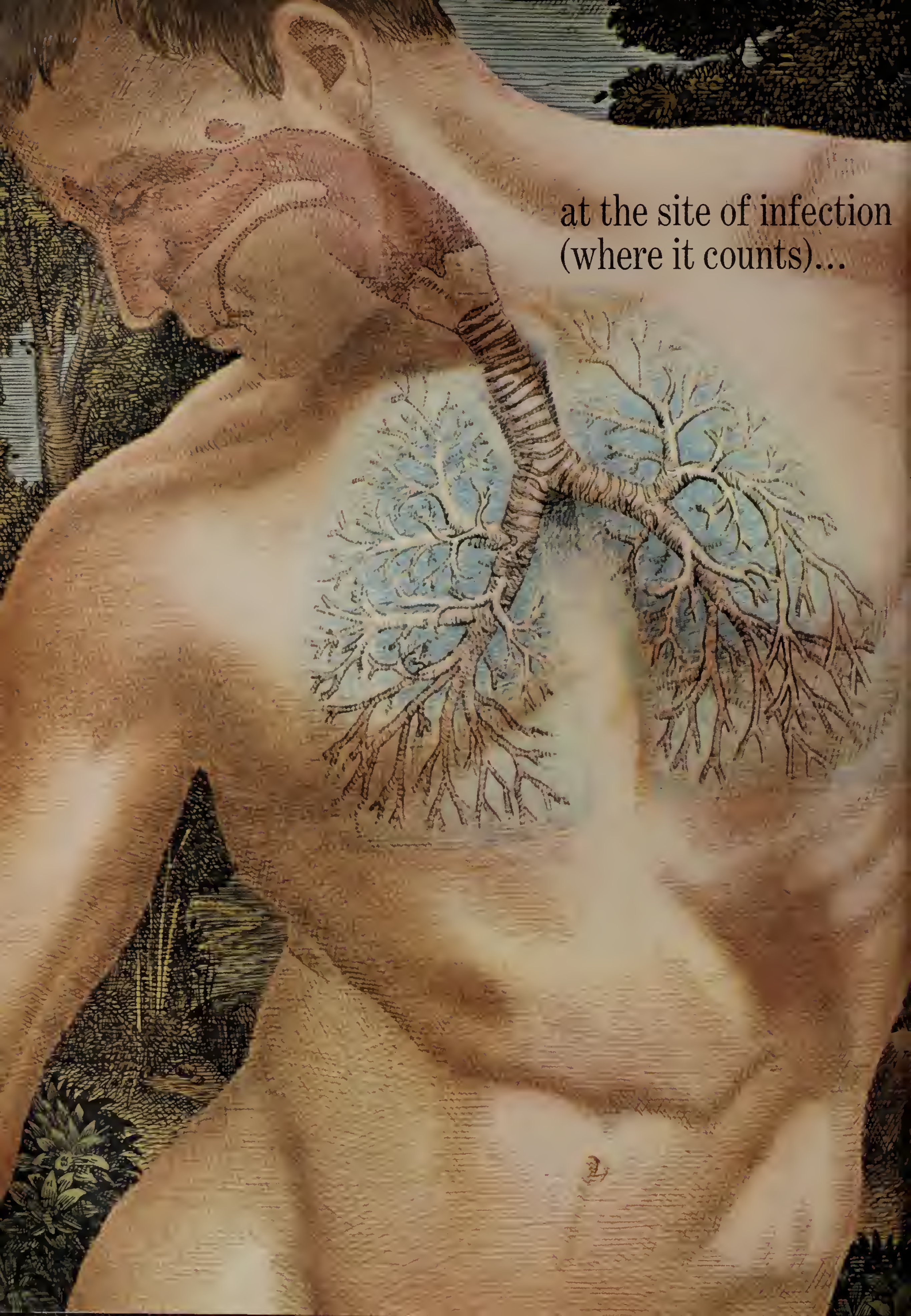
3 out of 4 painful shoulder patients responded well

Sperling, I.L.
Applied Therap. 6 117, 1964
84.2% of 127 patients

Rosenbaum, E.E., and Schwarz, G.R. Northwest Med. 61:927, 1962
81% of 48 patients

Please see adjoining page for brief prescribing summary.

TA-5094PC


at the site of infection
(where it counts)...

# Ilosone® provides more antibacterial activity than any other oral erythromycin

**Acid stable, better absorbed... Ilosone produces faster, higher, more prolonged blood levels, even in the presence of food[1-3]**

Because it is the most active form of oral erythromycin, Ilosone can help assure consistently greater antibacterial activity at the site of infection. Ilosone produces peak antibacterial blood levels two to four times those of other erythromycin preparations.[1,2] Not only are these levels attained earlier, but they are maintained for much longer periods. Even the presence of food does not seem to affect the activity of Ilosone.[1,3]

In the treatment of patients with bacterial infections susceptible to erythromycin, Ilosone has compiled an excellent therapeutic record. Since it exerts its greatest activity against gram-positive organisms, it is particularly useful in common respiratory and soft-tissue bacterial infections. Ilosone kills—not merely inhibits—streptococci, pneumococci, and more strains of staphylococci than any other macrolide antibiotic. This bactericidal action, coupled with the high antibacterial levels attained, makes Ilosone especially valuable in patients with low host resistance, such as infants, debilitated individuals, and diabetics.

Ilosone has shown no cross-resistance with penicillin and may be effective against organisms that have become resistant to that agent. Despite its high antibacterial activity, Ilosone has demonstrated a low incidence of side reactions. Blood dyscrasias, ototoxicity, and tooth staining have not been observed. Infrequent cases of drug idiosyncrasy, manifested by a cholestatic jaundice, have occurred, but there have been no known definite residual effects.

**Now available:**
New! Ready-mixed Ilosone Liquid 125! (Contains erythromycin estolate equivalent to 125 mg. erythromycin base per 5-cc. teaspoonful.)

700970

**Ilosone®**
**Erythromycin Estolate**

Lilly

*(See next page for prescribing information.)*

# Ilosone®/the most active oral form of erythromycin

**Description:** Ilosone is the most active form of oral erythromycin that has been developed. Because it is stable in acid, well absorbed, and excreted in lesser amounts in the bile, it provides faster, higher, and longer-lasting levels of antibacterial activity (ABA) in the serum, even when taken with food, than do comparable doses of erythromycin.

**Indications:** Ilosone is indicated in infections caused by microorganisms sensitive to its action (especially staphylococci, hemolytic streptococci, and pneumococci). The drug is therefore useful in a high proportion of bacterial diseases encountered in clinical practice and particularly in the treatment of bacterial infections of the upper and lower respiratory tract and soft tissues.

In the treatment of acute bacterial pharyngitis and tonsillitis, this antibiotic has promptly eradicated the bacteria (streptococci) and has produced a parallel prompt clinical improvement. There have been no group A beta-hemolytic streptococci resistant to this preparation. In beta-hemolytic streptococcus infections, treatment should be maintained for ten days to prevent the development of rheumatic fever or glomerulonephritis.

Erythromycin estolate has proved to be very effective in pneumococcus pneumonia and in acute bronchitis with pneumococci on culture. Bronchopneumonia and otitis media in children have responded well to its use.

The antibiotic has been used very successfully in staphylococcus infections. Good therapeutic results have been obtained in soft-tissue infections, abscesses, cellulitis, carbuncles, wound infections, and furunculosis.

In serious staphylococcus infections, erythromycin preparations should be used only in combination therapy with other antimicrobial agents. As is the case with any treatment regimen used in these severe conditions, surgical procedures should be performed when indicated, and large dosages of the antimicrobial agents should be employed. In this fashion, Ilosone has been effective in staphylococcus pneumonia, osteomyelitis, septicemia, empyema, and meningitis.

Multiple 500-mg. doses of the drug have also been useful in gonorrhea and syphilis. Since penicillin is the drug of choice for the treatment of syphilis and gonorrhea, erythromycin estolate should be employed for these infections only in patients with a history of penicillin allergy. Also, other infections due to susceptible bacteria in patients known to be hypersensitive to penicillin or other antibiotics may be considered for treatment with Ilosone.

**Contraindications:** Ilosone is contraindicated in patients with a known history of sensitivity to this drug and in those with preexisting liver disease or dysfunction.

**Adverse Reactions:** Data obtained from seven years' use of propionyl erythromycin ester and erythromycin estolate (Ilosone) indicate that hepatic dysfunction with or without clinical jaundice may occur during or following courses of therapy with the drug.

Changes in liver function tests in such cases have been indicative of intrahepatic cholestasis. The symptoms appear to be the result of a form of sensitization. The initial symptoms have developed in some cases after a few days of treatment but generally have followed one or two weeks of continuous therapy or several courses of the drug. Symptoms reappear promptly, usually within forty-eight hours, if the drug is readministered to sensitive patients. Eosinophilia was noted in peripheral blood counts. The findings readily subsided without apparent residual effects when treatment was discontinued. Recovery was delayed in one reported instance. The physician indicated in this case that either drug-induced jaundice or viral hepatitis may have been responsible for the findings.

In one clinical study involving ninety-three patients treated with the antibiotic, three cases of jaundice were observed and an additional eleven cases developed some changes in liver function tests. Three of the patients had abnormal liver function tests a second time on readministration of the drug.

Even though it is assumed that not all cases of jaundice have been reported, it seems clear that the number is small compared with the amount of drug that has been used. Reported cases have included persons in whom there had been administered other drugs known to be associated at times with hepatic side-effects and cases in which the presence of viral hepatitis or other disease may have been responsible for the findings. In some of the cases, associated gastro-intestinal symptoms simulated the colic of biliary tract disease. In other instances, clinical symptoms and results of liver function tests resembled findings in extrahepatic obstructive jaundice. It appears that the occurrence of jaundice after administration of Ilosone is infrequent, but further investigations are being made to estimate its incidence more accurately.

In those cases mentioned above in which jaundice appeare be definitely related to use of the drug, laboratory findings w characterized by increased direct-reacting bilirubin, eleva alkaline phosphatase levels, negative or weakly positive ceph flocculation and thymol turbidity tests, elevated serum gluta oxalacetic transaminase levels, peripheral eosinophilia, and mal cholecystograms.

Individual idiosyncrasy seems evident since jaundice has been reported in other patients taking prolonged courses of medication. Patients with chronic infection have been given to 2 Gm. of the drug daily for periods of two to six months, patients with rheumatic fever have taken prophylactic dose 0.5 Gm. daily for two years without difficulty. In one grou 144 patients who received the drug daily for two years, no ja dice was noted. It was of interest that members of six of th patients' families, who were not taking the drug, had episo of jaundice during the study period.

Transaminase and serum alkaline phosphatase levels w determined in a group of fifty-four adults and children who t 250 mg. of Ilosone daily for an average of sixteen months rheumatic fever prophylaxis. The results were compared those of a similar group of forty-four patients who received icillin. There were no cases of jaundice in either group. Eleva of SGPT and serum alkaline phosphatase levels during the co of treatment was observed in one patient treated with Ilos and in two patients treated with penicillin. Seven other pati in the group receiving Ilosone and four others in the penic group showed elevations in one of the tests at some time du administration of the drugs.

Very satisfactory therapeutic results, without toxicity, reported in 102 pediatric patients who received short-term ( day) courses of Ilosone in the treatment of streptococcus in tions. Results of liver function tests in these patients w comparable to those in a similar control group who had recei penicillin.

Gastro-intestinal disturbances not associated with hepatic fects are observed in a small proportion of individuals as a re of a local stimulating effect of the medication on the aliment tract; however, the normal intestinal gram-negative bacte flora is not appreciably altered by erythromycin drugs.

Although allergic manifestations are uncommon with the of erythromycin, there have been occasional reports of urtica skin eruptions, and, on rare occasions, anaphylaxis.

**Administration and Dosage:** Ilosone is administered orally.

Ilosone Pulvules®, Ilosone Liquid 125, Ilosone, 125, for ( Suspension, Ilosone Drops, Ilosone Chewable Tablets.

For infants and for children under twenty-five pounds of b weight, the usual dosage is 5 mg. per pound every six hours; children twenty-five to fifty pounds, 125 mg. every six ho (Tablets Ilosone Chewable should be chewed or crushed swallowed with water.)

For adults and for children over fifty pounds, the usual dos of Ilosone is 250 mg. every six hours.

For severe infections, these dosages may be doubled.

When larger doses are indicated, parenteral erythrom therapy should be considered.

In the treatment of syphilis, the recommended total dosag 20 to 30 Gm. given in divided doses for a period of ten to fif days. Close follow-up of the patient is necessary since eryt mycin drugs have not had adequate evaluation in all stage syphilis. Examinations of spinal fluid are recommended as of the follow-up therapy.

For gonorrhea, 500 mg. four times a day for four days recommended. In the treatment of gonorrhea, patients wi suspected lesion of syphilis should have a dark-field examina before receiving antibiotics, and monthly serologic tests sh be made for a period of three months.

**How Supplied:** Pulvules Ilosone, Capsules, N.F., 125 and 250 (equivalent to base), in bottles of 24 and 100.

Ilosone Liquid 125, Oral Suspension, U.S.P., 125 mg. (equiva to base) per 5-cc. teaspoonful, in 60-cc. and pint-size packa

Ilosone, 125, for Oral Suspension, N.F., 125 mg. (equiva to base) per 5-cc. teaspoonful, in 60 and 150-cc.-size packa

Ilosone Drops, 5 mg. (equivalent to base) per drop, in 10-cc.- packages, with dropper calibrated at 25 and 50 mg.

Tablets Ilosone Chewable, N.F., 125 mg. (equivalent to ba in bottles of 50.

[032

*References:* 1. Griffith, R. S., and Black, H. R.: Am. J. M. Sc., *247*:69,
2. Griffith, R. S., and Black, H. R.: Antibiotics & Chemother., *12*:398,
3. Hirsch, H. A., Pryles, C. V., and Finland, M.: Am. J. M. Sc., *239*:198, 1960.

*Additional information available to physicians upon request.*
*Eli Lilly and Company, Indianapolis, Indiana 46206.*

MEMO FROM . . .

to :

DR. "A"*
Administrator, Income Protection Plan,
Medical Society of the District of Columbia

# *"Thank you for relieving me of a financial burden"*

Dr. "A", Washington, D.C., was mighty thankful he had the Medical Society's Income Protection Plan when he was disabled recently by an accident.

Mutual of Omaha, underwriter of the plan, sent Dr. "A" a check for $2,562.60, paying him benefits under his Medical Society coverage as well as the supplementary coverage he has had with Mutual of Omaha since 1932.

All told, Mutual of Omaha has paid Dr. "A" a total of $8,003.38 in benefits since 1955. These checks, covering three separate disabilities, have helped him meet his financial obligations when he was unable to carry on his practice.

On each occasion Dr. "A" has been completely satisfied with the manner in which his applications for benefits have been handled and said so in a recent letter to Mutual of Omaha.

To put it in his own words: "I feel that my best friend in time of need has been Mutual of Omaha."

## Others Sing the Praises of Their Medical Society Protection Too:

### Dr. "B"*
### Laurel, Maryland

Since purchasing his Medical Society Income Protection Plan in 1953, Dr. "B" has been disabled five times. He has received benefit checks totaling $1,199.91. Says Dr. "B": "I can truly state that I am very satisfied with my policy with Mutual of Omaha and wish to express my sincere thanks."

### Dr. "C"*
### Washington, D. C.

When Dr. "C" received his benefit draft for $1,050.00 he commented that he was "most gratified to hear from Mutual of Omaha. Payment of sick benefits was made promptly, and was most appreciated at that time. I have nothing but praise for your organization and appreciate very much the privilege of holding a policy with you."

### Dr. "D"*
### Glenn Dale, Maryland

After receiving benefits five times for a total of $628.54, Dr. "D" has this to say about his Mutual of Omaha coverage: "I would not hesitate to recommend your company to any of my friends, and can understand why Mutual of Omaha was selected to underwrite the Medical Society's group plan."

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**Contraindications:** Infants, patients with history of convulsive disorders or glaucoma.
**Warning:** Not of value in the treatment of psychotic patients, and should not be employed in lieu of appropriate treatment.
**Precautions:** Limit dosage to smallest effective amount in elderly patients (not more than 1 mg, one or two times daily) to preclude ataxia or oversedation. Advise patients against possibly hazardous procedures until correct maintenance dosage is established; driving during therapy not recommended. In general, concurrent use with other psychotropic agents is not recommended. Warn patients of possible combined effects with alcohol. Safe use in pregnancy not established. Observe usual precautions in impaired renal or hepatic function and in patients who may be suicidal; periodic blood counts and liver function tests advisable in long-term use. Cease therapy gradually.
**Side Effects:** Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances, hallucinations); changes in EEG patterns. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.
**Dosage**—Adults: Mild to moderate psychoneurotic reactions, 2 to 5 mg b.i.d. or t.i.d.; severe psychoneurotic reactions, 5 to 10 mg t.i.d. or q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; muscle spasm with cerebral palsy or athetosis, 2 to 10 mg t.i.d. or q.i.d. Geriatric patients: 1 or 2 mg/day initially, increase gradually as needed.
**Supplied:** Tablets, 2 mg, 5 mg and 10 mg; bottles of 50 for convenience and economy in prescribing.

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(1) Siver, R. H.: CMD, *21*:109, September 1954. (2) Frykman, H. H.: Minn. Med., *38*:19-27, January 1955. (3) McGivney, J.: Tex. State Jour. Med., *51*:16-18, January 1955. (4) Quehl, T. M.: Jour. of Florida Acad. Gen. Prac., *15*:15-16, October 1965. (5) Weekes, D. J.: N.Y. State Jour. Med., *58*:2672-2673, August 1958. (6) Weekes, D. J.: EENT Digest, *25*:47-59, December 1963. (7) Abbott, P. L.: Jour. Oral Surg., Anes., & Hosp. Dental Serv., 310-312, July 1961. (8) Rapoport, L. and Levine, W. I.: Oral Surg., Oral Med. & Oral Path., *20*:591-593, November 1965.

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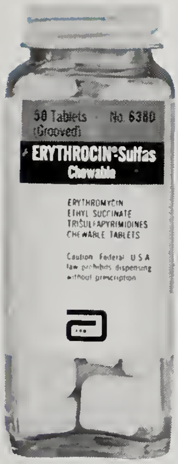
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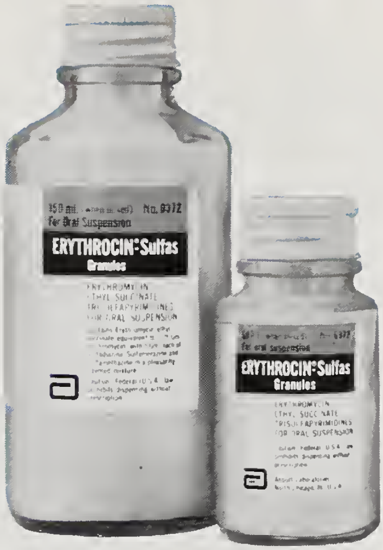
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1. Case Reports on File, Dept. Clin. Development, Abbott Laboratories.
2. Polley, R.F.L., Use of Erythromycin-Sulfas in Office Practice, Western Med., 7:177, July, 1966.

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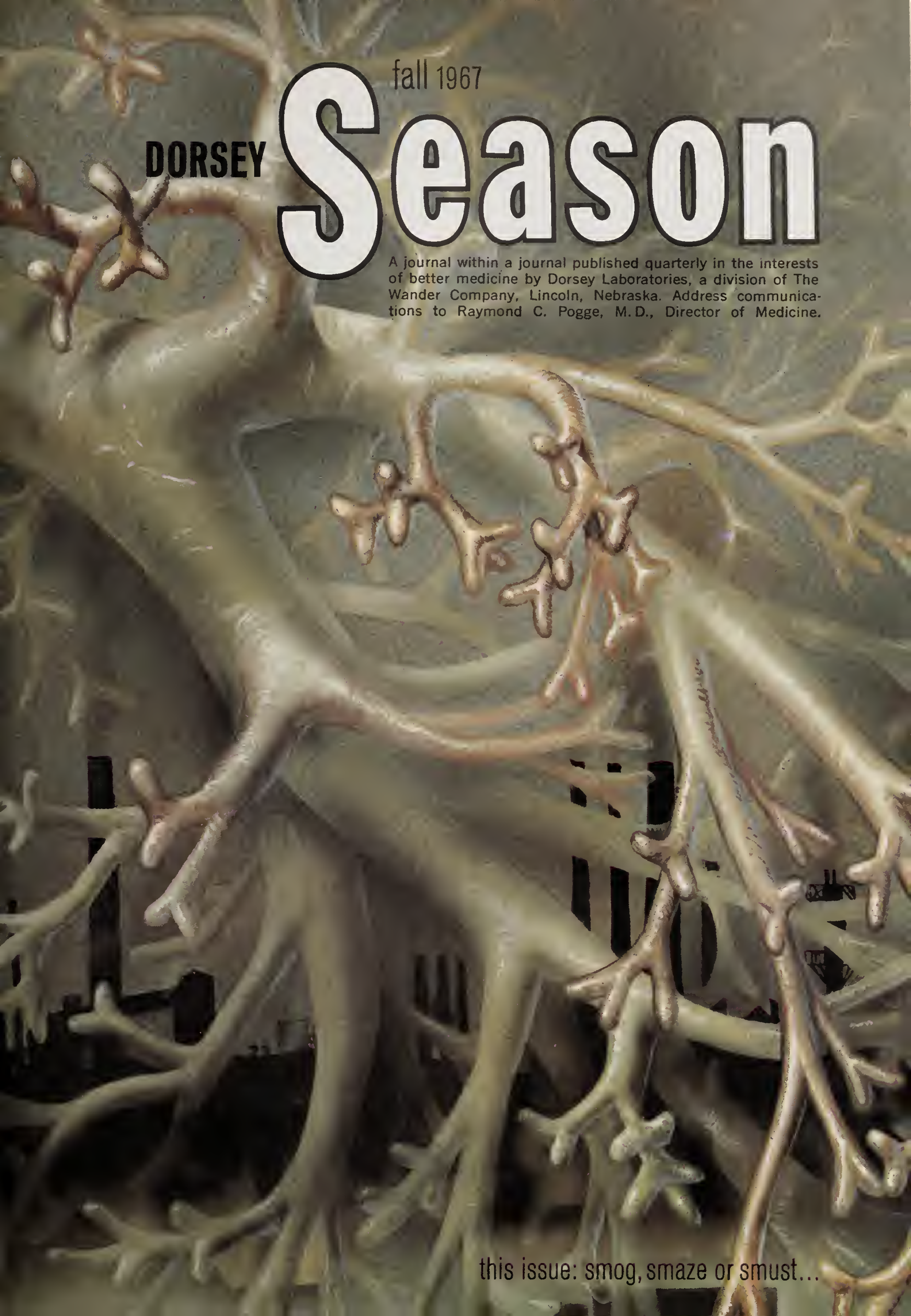


this issue: smog, smaze or smust...

# Smog, smaze or smust...effects of air pollution on upper respiratory tract

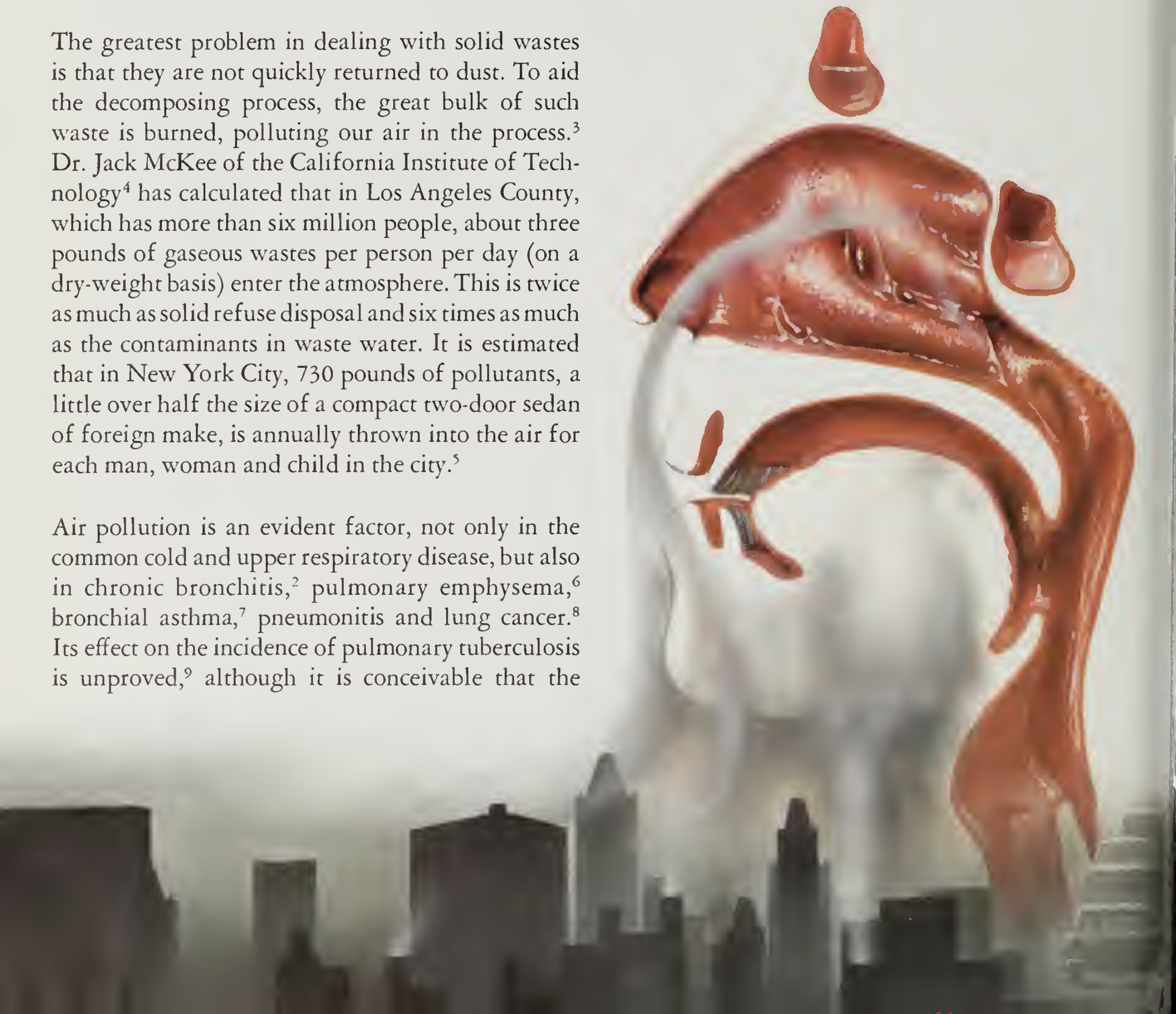
Nathan Flaxman, M.D., Diplomate, American Board of Internal Medicine, Chicago, Illinois

In Los Angeles it is *smog* (smoke and fog). In New York City *smaze* (smoke and haze). In El Paso *smust* (smoke and dust). The original factor was smoke plus such natural phenomena as fog, haze and dust, but air pollution has mushroomed from a smoke problem in our industrial cities into a major economic, esthetic and public health problem that affects practically every American locality and citizen.[1,2] Respiratory disease, of course, is by far the most costly effect of air pollution, for contaminated air can aggravate our illnesses, deplete our strength and shorten our life span.[1]

The greatest problem in dealing with solid wastes is that they are not quickly returned to dust. To aid the decomposing process, the great bulk of such waste is burned, polluting our air in the process.[3] Dr. Jack McKee of the California Institute of Technology[4] has calculated that in Los Angeles County, which has more than six million people, about three pounds of gaseous wastes per person per day (on a dry-weight basis) enter the atmosphere. This is twice as much as solid refuse disposal and six times as much as the contaminants in waste water. It is estimated that in New York City, 730 pounds of pollutants, a little over half the size of a compact two-door sedan of foreign make, is annually thrown into the air for each man, woman and child in the city.[5]

Air pollution is an evident factor, not only in the common cold and upper respiratory disease, but also in chronic bronchitis,[2] pulmonary emphysema,[6] bronchial asthma,[7] pneumonitis and lung cancer.[8] Its effect on the incidence of pulmonary tuberculosis is unproved,[9] although it is conceivable that the presence of various materials polluting the air might do this. A siege of smog in Denver, the "mile high city," in December 1965 was accompanied by respiratory infection that doubled normal absentee rates in schools, factories and city government.[10]

While air pollution is only one factor, it has become important in the causes of most of the afflictions of the respiratory tract. This has been shown not only by the Denver occurrence, but also by detailed study[2] of respiratory illness in a small group of 313 men



from October 1962 to May 1963 when there were 202 episodes involving the upper respiratory tract. The attack rate of illness was related in time to increased concentration of both smoke and sulphur dioxide in the atmosphere of the district in which the men lived.

Other factors often mentioned, include exposure to those who have colds, exposure to extreme changes of temperature, allergy and bacterial infection. However, when low individual resistance due to lack of rest, overwork, fatigue, improper or unbalanced diet, previous illness and emotional stress are included as causes, we enter the realm of somewhat obscure relationships. Much more emphasis can be placed on the role of polluted air.

the symptoms, signs and complications of involvement of the upper respiratory tract, especially the common cold, are the same regardless of the causative factor. Swelling of the lining of the nose, the scratchy dry throat, the discharge from the nose at first watery then thicker, discolored and more tenacious, the eyes tearing, and frequent sneezing are all part of the Number 1 human ailment. Concurrent or residual sinusitis when mucus is trapped there, middle ear involvement due to interference with drainage, laryngitis and bronchitis are complications of the common cold. The primary interference is with a most important function of the nose—the cleansing of foreign matter in the first line of "air defense" to prevent it from entering the breathing tract.

However, the diagnosis and subsequent decision on how to treat the patient so affected rests basically on the relief of symptoms that cause him the misery. The stuffed, runny nose, the clogged ears, and the harsh dry cough—all the symptoms that make common cold sufferers feel miserable and interfere with their sleep—can be alleviated with medications of the oral nasal decongestant/antihistamine combination type. The burning sensation in the throat, soreness of the chest and even chest pain can also be relieved by such medication. Rest in bed if there is fever (but confined to home at least), liberal fluids, uniformly warm surroundings and adequate humidity in the room, are all helpful adjuncts to the medication. Most common cold sufferers recover rapidly and are symptom-free in four to ten days.

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Further treatment, altered by the fact that the affliction hangs on for more than the usual duration of the common cold, requires consideration of allergy, which is most frequently the prolonging factor. But air pollution itself may often be the culprit.

*(Concluded on following page)*

At the Third National Conference on Air Pollution held recently, it was emphasized that this subject had received more attention in the past four years than in all previous history. Spicer,[11] an active participant at this conference, reiterated that it behooves the practicing physician to be aware of trends in respiratory disease and to accept a major role in community action relating to air pollution and respiratory health. By taking a positive stand physicians have been instrumental in the development of antipollution legislation. An outstanding example is Los Angeles where major steps have been taken by abolishing coal burning, and even banishing oil burning, seven months a year. Natural gas must be used instead and it must be used by industry when available. Backyard incinerators have been abolished in favor of landfill disposal, and building incineration ended except for a few expensive smokeless furnaces.[10] Concerted action can be taken against particular industrial nuisances. One company that disregarded complaints discovered its error when thousands of its credit cards were returned by irate customers who decided to patronize competing companies.[12]

*Summary.* Respiratory disease is the most important and most costly effect of air pollution, whether termed smog, smaze, or smust. Air pollution is an economic, esthetic and public health problem that affects practically every American locality and citizen. New sources of air pollution are invisible and odorless, but the harmful gases and liquid droplets are there. Triggered by sunlight, some of these undergo mid-air chemical changes and the results are even more irritating to the upper respiratory tract. The symptoms, signs and complications, especially of the upper respiratory tract, can be readily aborted by modern medication but may be unduly prolonged by polluted air. In steps taken to prevent this, the practicing physician can take a major role.

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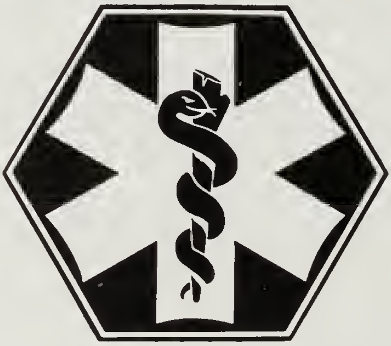
Emergency Medical Symbol



This is the universal emergency Medical Identification Symbol devised by the American Medical Association. The person who displays it carries upon his person information which should be known to anyone helping him during an accident or sudden illness. The symbol means: "Look for medical information that can protect life."

The World Medical Association has adopted the Emergency Medical Identification Symbol of the AMA as the "universal emergency medical information symbol."

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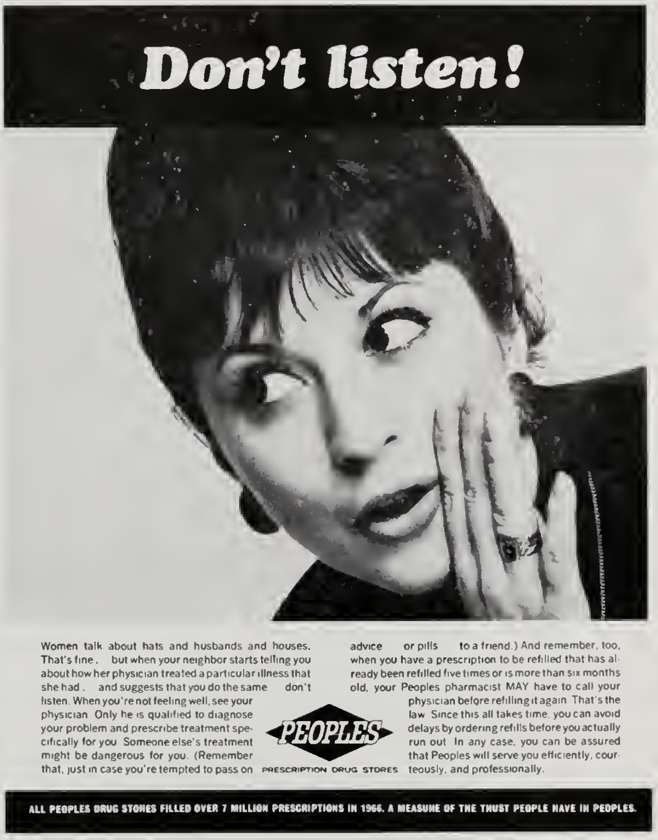
Just because Susie had the same symptoms, is it likely her neighbor needs the identical medication?



**Don't listen!**

Women talk about hats and husbands and houses. That's fine . but when your neighbor starts telling you about how her physician treated a particular illness that she had . and suggests that you do the same don't listen. When you're not feeling well, see your physician Only he is qualified to diagnose your problem and prescribe treatment specifically for you Someone else's treatment might be dangerous for you. (Remember that, just in case you're tempted to pass on advice or pills to a friend.) And remember, too, when you have a prescription to be refilled that has already been refilled five times or is more than six months old, your Peoples pharmacist MAY have to call your physician before refilling it again That's the law Since this all takes time, you can avoid delays by ordering refills before you actually run out In any case, you can be assured that Peoples will serve you efficiently, courteously, and professionally.

PEOPLES
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ALL PEOPLES DRUG STORES FILLED OVER 7 MILLION PRESCRIPTIONS IN 1966. A MEASURE OF THE TRUST PEOPLE HAVE IN PEOPLES.

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PEOPLES PRESCRIPTION DRUG STORES

**In the treatment of the anxious problem drinker:**

# when the need arises for a tranquilizer... consider Vistaril®

# HYDROXYZINE PAMOATE

**Actions:** Hydroxyzine is a rapid-acting, true ataraxic, unrelated chemically to phenothiazines, reserpine or meprobamate. It induces a calming effect in anxious, tense, psychoneurotic adults and also in anxious, hyperkinetic children without impairing mental alertness. It is not a cortical depressant, but its action may be due to a suppression of activity in certain key subcortical areas. Antihistaminic and antiemetic effects have been demonstrated clinically; skeletal and smooth muscle relaxation has been observed in experimental animals. It is rapidly absorbed in the gastrointestinal tract.

Hydroxyzine has demonstrated its clinical effectiveness in the chemotherapeutic aspect of the total management of neuroses and emotional disturbances manifested by anxiety, tension, agitation, apprehension or confusion.

**Indications:** Total management in conditions of emotional stress requires in most instances a combined approach of psychotherapy and chemotherapy. Hydroxyzine has been found to be particularly useful for this latter phase of therapy in its ability to render the disturbed patient more approachable and amenable to psychotherapy in long-term treatment of the psychoneurotic and the psychotic, although it should not be used as the sole treatment of psychosis or of clearly demonstrated cases of depression.

Hydroxyzine is also useful in alleviating the manifestations of anxiety and tension in situations in which the causative stress is temporary, as in the preparation for dental and other minor surgical procedures, and in acute emotional problems. It has also been recommended for the management of anxiety associated with organic disturbances such as certain types of heart disease, digestive disorders, dermatoses, senility, the menopausal syndrome, and behavior problems in brain-damaged or epileptic children.

In addition, it has been recommended as adjunctive therapy in alcoholism, and allergic conditions with strong emotional overlay, as in asthma, chronic urticaria, and pruritus.

Hydroxyzine has also demonstrated effectiveness in controlling nausea and vomiting associated with gastritis, gastroenteritis and enteritis; upper respiratory infections, influenza and pneumonia; postoperative conditions; miscellaneous diseases such as Ménière's syndrome, migraine, and vestibulitis.

Hydroxyzine for intramuscular use is especially useful in treating the acutely disturbed or hysterical patient and the acute or chronic alcoholic patient with anxiety withdrawal symptoms or delirium tremens. Used adjunctively pre- and postoperatively and pre- and postpartum, hydroxyzine allays anxiety, permits substantial reduction in narcotic dosage and controls emesis.

Clinical use of hydroxyzine as an adjunct to the management of labor has been extensively reported in the literature without evidence of harm to the mother or fetus.

**Contraindications:** Hydroxyzine, when administered to the pregnant mouse, rat, and rabbit induced fetal abnormalities in the rat at doses substantially above the human therapeutic range. Clinical data in human beings are inadequate to establish safety in early pregnancy. Until such data are available, hydroxyzine is contraindicated in early pregnancy.

Hydroxyzine is contraindicated in any individual who has shown a previous hypersensitivity to it. The parenteral solution is intended only for intramuscular or intravenous administration and should not, under any circumstances, be injected subcutaneously or intra-arterially.

**Precautions:** Drowsiness may occur with oral or parenteral use of this drug , and patients should therefore be warned of this possibility and cautioned against driving a car or operating dangerous machinery.

Since hydroxyzine may potentiate the action of central nervous system depressants, conjunctive use with these drugs requires that their dosage be decreased. Hydroxyzine reduces the requirements by as much as 50% for narcotics such as meperidine, so their use in preanesthetic adjunctive therapy should be modified on an individual basis.

As with any preparation for intramuscular injection, Vistaril (hydroxyzine hydrochloride) Parenteral Solution should be injected well within the body of a relatively large muscle such as in the upper outer quadrant of the buttock or the lateral thigh. To avoid the possibility of radial nerve injury, injections should not be made into the lower and middle thirds of the upper arm. Aspiration and proper anatomical selection of injection site should be observed as a precaution against inadvertent injection into a blood vessel or major nerve. In a few instances of reported intravenous administration of hydroxyzine hydrochloride, digital gangrene has occurred distal to the injection site, apparently the result of endarteritis and thrombosis. This event has been considered due to inadvertent intra-arterial injection, although the possibility of periarterial extravasation, with arterial spasm, cannot be ruled out. Therefore, particular caution should be observed when hydroxyzine parenteral solution is administered intravenously to insure that it is injected only into intact veins; avoid either intra-arterial injection or extravasation. Due to infrequent phlebitis resulting from too rapid intravenous administration of the solution, the rate of injection should not exceed 25 mg. per minute. A single intravenous administration in excess of 100 mg. is not recommended (see Adverse Reactions).

**Adverse Reactions:** No serious side effects have been reported and confirmed in the administration of hydroxyzine to date. While therapeutic doses of hydroxyzine seldom produce impairment of mental alertness, transient drowsiness may occur; this may disappear in a few days of continued therapy or upon dosage reduction. Dryness of the mouth may be seen with higher doses. Involuntary motor activity, including rare instances of tremor and convulsions, has been reported, usually with doses considerably higher than those recommended. Extensive clinical use has substantiated the absence of toxic effects on the bone marrow or liver when hydroxyzine was administered in recommended doses for over four years of uninterrupted therapy.

When this product is given intravenously undiluted, minimal amounts of intravascular hemolysis occur at the site of injection. Giving the maximum recommended intravenous dose (100 mg.) to adults results in immediate transient hemolysis with the liberation of a total of 2-3 grams of hemoglobin, which, in some individuals, can cause small amounts of hemoglobinuria. (In the course of normal red cell destruction in the body, approximately 8 Gm. of hemoglobin are liberated every 24 hours.) Therefore, it is recommended that, when given intravenously, parenteral hy-

*(Continued on succeeding page.)*

*Since 1849* Pfizer *Science for the world's well-being®*

PFIZER LABORATORIES Division, Chas. Pfizer & Co., Inc.
New York, N.Y. 10017

**when the need arises for a tranquilizer...consider**

**Vistaril**

HYDROXYZINE PAMOATE

*(Continued from preceding page.)*

droxyzine be diluted with 50 cc. of normal saline and given during a period of four minutes or more; with this technique, drug-induced hemolysis is unlikely.

Dosage: *Oral*—Adults: Dosage varies with individual requirements and ranges from 25 mg. t.i.d. to 100 mg. q.i.d.

Children: *under 6 years,* 50 mg. daily in divided doses; *over 6 years,* 50-100 mg. daily in divided doses.

*Parenteral*—For adult psychiatric and emotional emergencies, including acute alcoholism—I.M.: 50-100 mg. Stat., and q. 4-6 h., p.r.n.; I.V.: 50 mg. Stat., maintain with 25-50 mg. I.V. q. 4-6 h., p.r.n.

Nausea and vomiting—Adults: 25-100 mg. I.M. or I.V.; Children: 0.5 mg./lb. body weight I.M.

Pre- and postoperative adjunctive medication—Adults: 25-100 mg. I.M. or I.V.; Children: 0.5 mg./lb. body weight I.M.

Pre- and postpartum adjunctive therapy—25-100 mg. I.M. or I.V.

Patients may be started on parenteral therapy when indicated by the clinical situation. They should be maintained on oral therapy whenever this route is again practicable.

As with all potent medications, the dosage should be adjusted according to the patient's response to therapy.

Supply: *Vistaril (hydroxyzine pamoate) Capsules*—25 mg., two-tone green capsules; 50 mg., green-and-white capsules; and 100 mg., green-and-gray capsules; in bottles of 100 and 500. Each capsule contains hydroxyzine pamoate equivalent to 25 mg., 50 mg., or 100 mg. of hydroxyzine HCl.

*Vistaril (hydroxyzine pamoate) Oral Suspension*—Equivalent to 25 mg. hydroxyzine HCl per 5 cc. teaspoonful, in 1 pint bottles.

*Vistaril (hydroxyzine HCl) Parenteral Solution*—10 cc. vials, 25 and 50 mg. per cc.; 2 cc. vials, 50 mg. per cc., in packages of 6 vials; Isoject,® 25 and 50 mg. per cc., 1 cc. per unit. Isoject, 100 mg. per 2 cc. unit, 50 mg. per cc.

Composition (Parenteral Solution)

| Each cc. contains: | 25 mg./cc. | 50 mg./cc. |
|---|---|---|
| Hydroxyzine hydrochloride | 25 mg. | 50 mg. |
| Benzyl alcohol | 0.9% | 0.9% |
| Sodium hydroxide (approx.) to adjust to optimum pH | 0.22% | 0.46% |
| Water for Injection | q.s. | q.s. |

*More detailed professional information available on request.*

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## NATIONAL AND REGIONAL MEETINGS

September 25: Society for Pediatric Radiology. Washington Hilton Hotel, Washington. Address: Dr. John L. Gwinn, Secretary-Treasurer, Children's Hospital, 4614 Sunset Blvd., Los Angeles, Calif. 90027.

September 26–29: American Roentgen Ray Society. Washington Hilton Hotel, Washington. Address: Dr. Ted F. Leigh, Secretary, Emory University Clinic, Atlanta, Ga. 30322.

October 2–6: American College of Surgeons (Annual Meeting). Conrad Hilton Hotel, Chicago. Address: Dr. John Paul North, Director, 55 East Erie Street, Chicago, Ill. 60611.

October 4 and Wednesdays ff.: Series of Postgraduate Seminars on Clinical Psychiatry for the Practicing Physician. Georgetown University Hospital, Washington, on Wednesdays, 4–6 p.m. for 12 weeks. Address: Dr. Donald F. Bogdan, Department of Psychiatry, Georgetown University Hospital, Washington, D.C. 20007

October 6–8: American Association of Marriage Counselors. Washington Hilton Hotel, Washington. Address: Mrs. Patricia Schiller, 4224 38th Street, N.W., Washington, D.C. 20016.

October 18–19: Symposium on The Dermatology of the Negro. Howard University College of Medicine, Washington. Address: Dr. John A. Kenney, Jr., Chairman, Division of Dermatology, Freedmen's Hospital, Washington, D. C. 20001.

October 19–21: Medical Society of Virginia. Marriott Twin Bridges Motor Hotel, Alexandria, Va. Address: Mr. Robert I. Howard, Executive Secretary, 4205 Dover Road, Richmond, Va. 23221.

October 21–25: American Association of Blood Banks. Americana Hotel, New York. Address: Miss Lois J. James, 30 North Michigan Avenue, Chicago, Ill. 60602.

October 21–26: American Academy of Pediatrics. Washington Hilton Hotel, Washington. Address: Dr. E. H. Christopherson, Executive Secretary, 1801 Hinman Avenue, Evanston, Ill. 60204.

October 22–23: American College of Preventive Medicine. Fontainebleau Hotel, Miami Beach, Fla. Address: Dr. E. A. Piszczek, Executive Secretary, 6410 North Leona Avenue, Chicago, Ill. 60646.

October 23: American Association of Poison Control Centers. Washington Hilton Hotel. Washington. Address: Dr. Matilda S. McIntire, Secretary, Children's Memorial Hospital, 44th and Dewey Avenue, Omaha, Nebr. 68105.

October 30–November 14: Medical Seminar Caribbean Cruise sponsored by Georgetown University School of Medicine. *S. S. France,* New York. Address: Allen Travel Service, Inc., 565 Fifth Avenue, New York, N.Y. 10017.

November 20–22: Annual Scientific Assembly, The Medical Society of the District of Columbia. Statler-Hilton Hotel, Washington. Address: Mr. George W. Cooley, Executive Director, 2007 Eye Street, N.W., Washington, D. C. 20006.

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**Recommended by the Medical Society of D.C.**

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A COMPUTER CAN IMPROVE YOUR BILLING SYSTEM and Afford Substantial Savings to Your Office.

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10. **No extensive training of personnel required.** We will train and retrain as part of our service.
11. **No expensive equipment to buy, maintain, rent or operate.**

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*This service is supervised and controlled by a Board of Doctors appointed by the Medical and Dental Societies of D.C.*

**Call The Medical Society for Further Information—223-2236**

## What can be done for Susan Jane To stop the runs and crampy pain?

Parepectolin for quick relief of acute diarrhea
...soothes colicky pain with paregoric
...consolidates fluid stools with pectin
...adsorbs irritants with kaolin, and protects intestinal mucosa.

In children, Parepectolin may be used to control diarrhea promptly and prevent dehydration, until etiology has been determined. In some cases, Parepectolin may be all the therapy necessary.

**Parepectolin®**

Each fluid ounce of creamy white suspension contains:
Paregoric (equivalent).........(1.0 dram) 3.7 ml.
Contains opium (¼ grain) 15 mg. per fluid ounce.
*warning: may be habit forming*
Pectin ..................... (2½ grains) 162 mg.
Kaolin (specially purified)....(85 grains) 5.5 Gm.
(alcohol 0.69%)
Usual Children's Dose: One or two teaspoonfuls three times daily.

WILLIAM H. RORER, INC.
Fort Washington, Pa.

## Why Vascular Specialists Prescribe JOBST Supports

The JOBST VENOUS PRESSURE GRADIENT support is fitted by precise measurements to the contour of the affected limb of the individual patient and exerts precise hydrostatic counter pressures. JOBST supports represent an advanced clinical method of treatment known and accepted by most vascular specialists as the *treatment of choice* for leg ulcers, varicose veins, stasis dermatitis, postmastectomy lymphedema, post phlebitis syndrome, post-fracture, post-operative and injury edema. Trained experts will measure and fit your patients for you at the JOBST Service Centers: Suite 200, 818 Eighteenth St., N.W., Washington, D. C., Ph. 298-5530 and Suite 415, Medical Arts Bldg., 101 W. Read St., Baltimore, Ph. 539-0560.

© JOBST, 1966

JOBST offers a complete range of custom-made support garments for the treatment of venous insufficiency and management of lymphedema.

# A Building Block approach to treating hypertension

ABBOTT

**With these three therapeutic building blocks you can create a once-a-day regimen to fit almost any degree of hypertension. See the following pages for details . . .**

Pargyline Hydrochloride
Deserpidine
Methyclothiazide
180
160
140
120
100
80

# Consider starting your hypertensives on this basic thiazide

ABBOTT

**A single daily dose of Enduron provides sodium excretion around the clock**

Enduron is a true 24-hour single-dose thiazide. Its sodium excretion is not squeezed into an abrupt peak during the first several hours. It is well-sustained in a plateau-like effect—with little reduction for the first 12 hours, and decline thereafter only gradual.

Potassium loss, by contrast, is low. It reaches an early minor peak, then subsides rapidly. Moreover, since dosage is but once a day, there is but one daily peak of potassium loss. As with all thiazides, however, dietary potassium supplementation should also be considered, especially in long or intensive therapy.

Use Enduron as an ideal starting therapy in mild hypertension. Use it too, as a basic therapeutic building block with which other agents can be joined, for managing your more resistant hypertensives.

*Once a day, every day*

ENDURON®
METHYCLOTHIAZIDE

ENDURON
ENDURON
METHYCLO-THIAZIDE
2.5 mg
Methyclothiazide

| | Minimum | Usual | Intermediate | Maximum |
|---|---|---|---|---|
| DAILY DOSAGE RANGE | | | | |
| | 2.5 mg. tablet | 5 mg. tablet | 7.5 mg. | 10 mg. |

*See Brief Summary on final page of advertisement.*

# To build added response, shift to Enduronyl

ABBOTT

## The deserpidine component adds enhanced antihypertensive activity

The rauwolfia component of Enduronyl is deserpidine (Harmonyl®), a purified crystalline alkaloid supplied only by Abbott. It augments Enduron with its own antihypertensive and tranquilizing action.

Thus the combined clinical effect of these two therapeutic building blocks in Enduronyl is greater than can ordinarily be achieved with either alone.

To add flexibility, Enduronyl comes in two strengths: regular and Forte. Both provide 5 mg. of Enduron. The variation is where most helpful: in the deserpidine. The tablets are scored, and give a surprisingly wide and economical choice of once-a-day doses (see below).

Choose Enduronyl for your patients in the broad range of mild to moderate hypertension. Patient acceptance is excellent!

Deserpidine
Methyclothiazide

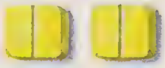
*Once a day, every day*

**ENDURONYL®**

METHYCLOTHIAZIDE 5 MG. WITH DESERPIDINE 0.25 MG.

**ENDURONYL FORTE**

METHYCLOTHIAZIDE 5 MG. WITH DESERPIDINE 0.5 MG.

| | Minimum | Usual | Intermediate | Maximum |
|---|---|---|---|---|
| DAILY DOSAGE RANGE | <br>2.5 mg. methyclothiazide<br>0.125 mg. deserpidine | <br>5 mg. methyclothiazide<br>0.25 mg. deserpidine | <br>7.5 mg. methyclothiazide<br>0.375 mg. deserpidine | <br>10 mg. methyclothiazide<br>0.5 mg. deserpidine |
| DAILY DOSAGE RANGE | <br>2.5 mg. methyclothiazide<br>0.25 mg. deserpidine | <br>5 mg. methyclothiazide<br>0.5 mg. deserpidine | <br>7.5 mg. methyclothiazide<br>0.75 mg. deserpidine | <br>10 mg. methyclothiazide<br>1 mg. deserpidine |

*See Brief Summary on final page of advertisement.*

# Eutonyl affords a different kind of basic therapy for moderate to severe cases

## Effect tied to reduced peripheral vascular resistance; no central depressant action

Eutonyl is a unique nonhydrazine agent. It is reported to act by reducing peripheral vascular resistance.[1,2]

In clinical trials, significant reductions in mean blood pressure were seen in 84% of patients studied—all were moderate to severe cases. Eutonyl lowers diastolic in proportion to systolic, and in about half of the cases studied, reductions in the sitting and recumbent positions were nearly as great as in the standing position.

Most important: There is no central depressant action. In fact, some patients reported an *increased* sense of well being.

Here, then, is a highly effective *basic treatment* for moderate to severe cases—and one that will not hamper your patient with lethargy or drowsiness while on treatment.

*Once a day, every day*

**EUTONYL®**
PARGYLINE HYDROCHLORIDE

EUTONYL®
EUTONYL®
25 PARGYLINE HYDROCHLORIDE
EUTONYL®
50 PARGYLINE HYDROCHLORIDE
Pargyline Hydrochloride

| DAILY DOSAGE RANGE | Minimum | Usual starting | Intermediate | Maximum |
|---|---|---|---|---|
| | <br>10 mg. tablet | <br>25 mg. tablet | <br>50 mg. tablet<br>or as needed | <br>200 mg. |

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1. *Brest, A. N., et al., Cardiac and Renal Hemodynamic Response to Pargyline, Ann. N. Y. Acad. Sci., 107-1016, 1963.*
2. *Winsor, T., Pargyline Hydrochloride, Hypertension, Urinary Tryptamine, and Vascular Reflexes, Geriatrics, 19:598, Aug., 1964.*

*See Brief Summary on final page of advertisement.*

# Eutron adds thiazide for enhanced therapy with milder side effects

ABBOTT

**Only a 7/4 mm. span between standing and recumbent pressures in clinical trials—reduced chance of orthostatic hypotension**

The combining of Eutonyl and Enduron in Eutron permits a significantly greater antihypertensive effect than with either agent used alone. This in turn may allow therapeutic success with lesser dosage—and correspondingly milder side effects.

A significant finding in clinical trials was the drug's action in lowering blood pressure to *nearly equal levels in all body positions*. Total average spread between standing and recumbent readings (after treatment) was only 7/4 mm. Hg.

Thus, in your moderate to severe cases, Eutron affords a usually smooth course of therapy, often with reduced likelihood of orthostatic effects. (The usual precautions against rising suddenly, of course, will always apply.) And, because of the thiazide component, Eutron may be used in the presence of congestive heart failure.

EUTRON
Methyclothiazide
Pargyline Hydrochloride

*Once a day, every day*

**EUTRON™**

PARGYLINE HYDROCHLORIDE 25 MG.
WITH METHYCLOTHIAZIDE 5 MG.

| | Minimum | Usual starting | Intermediate | Maximum |
|---|---|---|---|---|
| DAILY DOSAGE RANGE | | | | |
| | 12.5 mg. pargyline hydrochloride and 2.5 mg. methyclothiazide | 25 mg. pargyline hydrochloride and 5 mg. methyclothiazide | 37.5 mg. pargyline hydrochloride and 7.5 mg. methyclothiazide | 50 mg. pargyline hydrochloride and 10 mg. methyclothiazide |

*See Brief Summary on final page of advertisement.*

TM—Trademark

707075-R

## ENDURON®

**METHYCLOTHIAZIDE**

## ENDURONYL®

Each tablet contains
Methyclothiazide 5 mg. with
Deserpidine 0.25 mg. or 0.5 mg.

*Indications:* Enduron is used to control edema and mild to moderate hypertension; also used with other drugs for hypertension. Enduronyl is used in mild to moderately severe hypertension; when used with Enduronyl, more potent agents can be given at reduced dosage to minimize undesirable side effects.

*Contraindications:* Neither Enduron nor Enduronyl should be used in severe renal disease (except nephrosis) or shutdown; in severe hepatic disease or impending hepatic coma; in patients sensitive to thiazides. Hepatic coma has been reported as a result of hypokalemia in patients receiving thiazides.

Enduronyl is contraindicated in patients with severe mental depression and suicidal tendencies, active peptic ulcer, or ulcerative colitis.

*Warnings:* Consider possible sensitivity reactions in patients with a history of allergy or asthma. If added potassium intake is indicated, dietary supplementation is recommended. Enteric-coated potassium tablets should be reserved for cautious use only when adequate dietary supplementation is not practical because those tablets may induce serious or fatal small bowel lesions consisting of stenosis with or without ulceration. These small bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs.

*Precautions:* Use thiazides with caution in severe renal dysfunction, impaired hepatic function, or progressive liver disease. In surgical patients, thiazides may reduce the response to vasopressors and increase the response to tubocurarine. Use thiazides with caution in pregnancy (bone marrow depression, thrombocytopenia, or altered carbohydrate metabolism have been reported in certain newborn infants). Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. Antihypertensive response may be enhanced following sympathectomy.

Use Enduronyl with caution in patients with a history of peptic ulcer, as rauwolfias may increase gastric secretion. Discontinue at the first sign of mental depression. Rauwolfia alkaloids may increase hypotensive effects of surgery or anesthesia, and should be discontinued two weeks prior. They also lower the convulsive threshold and shorten seizure latency. In epilepsy, dosage adjustment of anticonvulsant medication may be necessary. Alcohol, barbiturates, or narcotics may potentiate action of deserpidine.

*Adverse Reactions:* During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). All patients should be observed for signs of hyponatremia ("low-salt" syndrome). Reported thiazide reactions include: anorexia, nausea, vomiting, diarrhea, headache, skin rash, dizziness, paresthesia, weakness, photosensitivity, jaundice, and pancreatitis.

Reported rauwolfia reactions include: nasal stuffiness, nausea, weight gain, diarrhea, aggravation of peptic ulcer, epistaxis, skin eruption, and reduction of libido and potency. Excessive drowsiness, fatigue, weakness, and nightmares may signal early signs of mental depression.

## EUTONYL®

**PARGYLINE HYDROCHLORIDE**

## EUTRON™

Each tablet contains
Pargyline Hydrochloride 25 mg.
with Methyclothiazide 5 mg.

*Indications:* For treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. Not recommended for patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone. It is desirable to establish the dosage of Eutron by administering component drugs separately.

TM-Trademark.

*Contraindications:* Pheochromocytoma, advanced renal disease, increasing renal dysfunction, paranoid schizophrenia and hyperthyroidism. Hepatic coma has been reported as consequence of hypokalemia with thiazide therapy. Until further experience is gained not recommended for patients with malignant hypertension, children under 12, or pregnant patients.

Concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. 2 week interval should separate therapy and use of these agents.

Methyclothiazide is contraindicated in patients with known sensitivity to thiazides.

*Warnings:* Pargyline hydrochloride is a monoamine oxidase inhibitor. Warn patients against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When indicated, alcohol, narcotics (meperidine should be avoided), antihistamines, barbiturates, chloral hydrate, and other hypnotics, sedatives, tranquilizers, or caffeine, may be used cautiously in reduced dosage. In emergency surgery ¼ to ⅕ the usual dose of narcotics, analgesics, and other premedications should be used avoiding parenteral administration where possible. Carefully adjust dose of anesthetics to response of patient. Withdraw pargyline two weeks before elective surgery.

Warn patients about the possibility of postural hypotension. Those with angina or coronary artery disease should not increase physical activity with an improvement in well being. Pargyline may lower blood sugar.

Avoid use of enteric-coated potassium tablets, as these may induce serious or fatal small-bowel lesions consisting of stenosis with or without ulceration. These small-bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs. These products contain no added potassium salts and if added potassium intake is desired, dietary supplementation is recommended. Coated potassium tablets should be reserved for cautious use when adequate dietary supplementation is impractical. In patients with a history of allergy or asthma the possibility of sensitivity reactions should be considered.

*Precautions:* Measure blood pressure while patient is standing to determine antihypertensive effect. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Use with caution in patients with liver disease. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. With prolonged therapy, examine patients for change in color perception, visual fields and fundi. Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. In surgical patients thiazides may reduce response to vasopressors and increase response to tubocurarine.

*Adverse Reactions:* Pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extrapyramidal symptoms have been reported in a few patients with reduced cardiac reserve.

During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). Observe all patients for signs of hyponatremia ("low salt" syndrome).

Reported thiazide reactions also include anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, and pancreatitis. Nocturia has been observed with the combination.

709075R

ABBOTT

# New view of an oral contraceptive at work

Although suppression of ovulation remains the primary mode of action of oral contraceptives, newer knowledge indicates that products like Norinyl-1— a combination of both low-dosage progestogen and estrogen for the full treatment cycle—may provide multiple action that helps explain their unexcelled record of contraceptive effectiveness. This report explores the possible secondary protective mechanisms offered by combined hormonal administration.

Accumulating evidence has indicated that sparse, highly viscous cervical mucus has a possible adverse effect on the motility and survival of spermatozoa.

The estrogen-opposing progestational ingredient of Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.) changes the usual midcycle picture of a thin, watery cervical mucus. The result—a built-in barrier that appears to inhibit sperm from reaching the ovum should one be released. The inset in the adjoining photograph shows immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

See last page for contraindications, precautions, side effects and dosage.

# How the estrogen-opposing action of Norinyl-1 creates cervical mucus that may be hostile to sperm penetration

Normally, estrogen activity during the fertile midcycle stimulates the production of a profuse and watery cervical mucus that permits maximum sperm motility and promotes penetration.

But what happens when Norinyl-1 is administered? Its potent progestogen, norethindrone, opposes estrogen stimulation of cervical mucus. Consequently, the amount of mucus decreases and its viscosity increases. This results in a sparse but thick mucus barrier that appears to diminish the vitality of the sperm and to impair its powers of penetration.

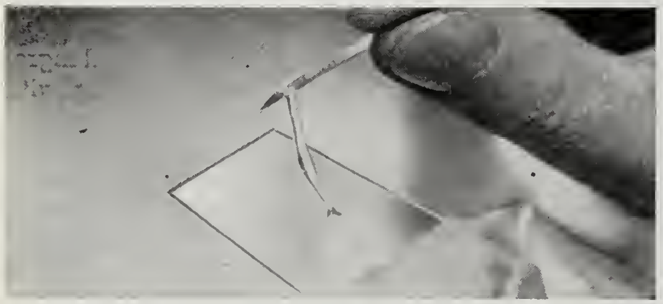
## The role of viscous cervical mucus as a secondary action of Norinyl-1

In a report on 89 patients taking this medication,* cervical mucus obtained from cycle day 5 to cycle day 29 appeared scant and thick and exhibited little or no Spinnbarkeit.

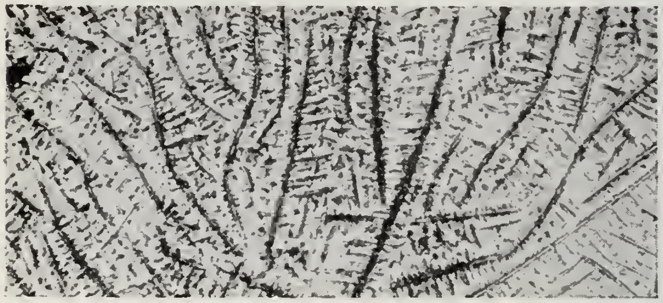
In the opinion of this investigator, the effect on cervical mucus may be sufficient to prevent conception.

*Cohen, M. R.: Symposium: Mechanisms of Action of Low Dosage Oral Contraceptive, Yale University Medical Center, New Haven, Conn., April 6, 1967.

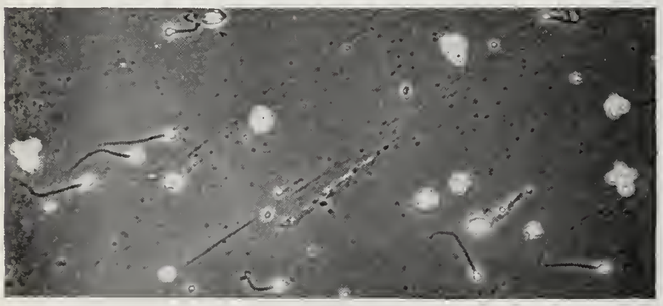
### Normal cervical mucus at midcycle in untreated patient is known to permit sperm motility... promote sperm penetration.



Cervical mucus is thin and watery with a stretchability (Spinnbarkeit) of 15 to 20 cm.

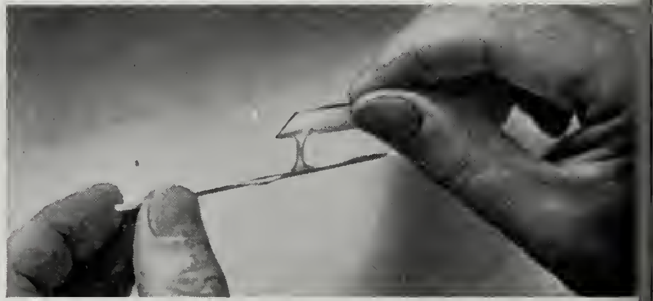


Thin, watery mucus crystallizes into this well-defined, fernlike pattern within a minute.

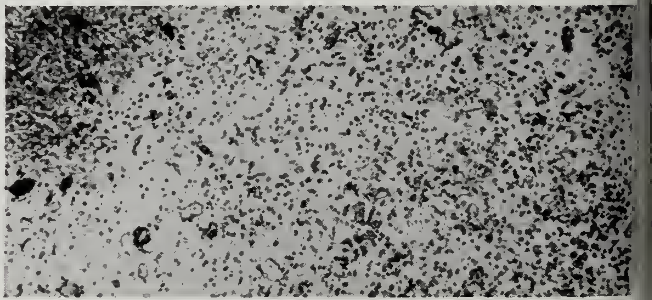


Spermatozoa appear healthy, are active and freemoving.

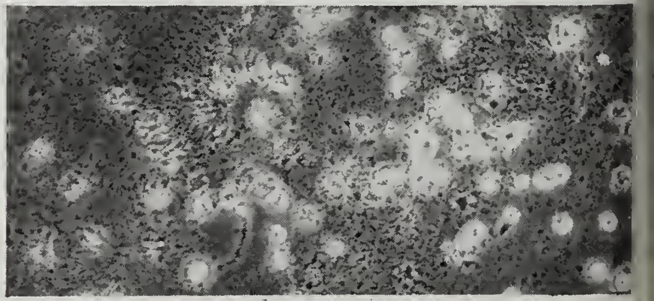
### Viscous cervical mucus at midcycle produced by Norinyl-1 appears to impair sperm vitality... inhibit penetration.



Cervical mucus is scanty, thick and viscous. Spinnbarkeit is 1 cm. or less.



In thick, viscous cervical mucus the fern pattern is poorly defined or absent.

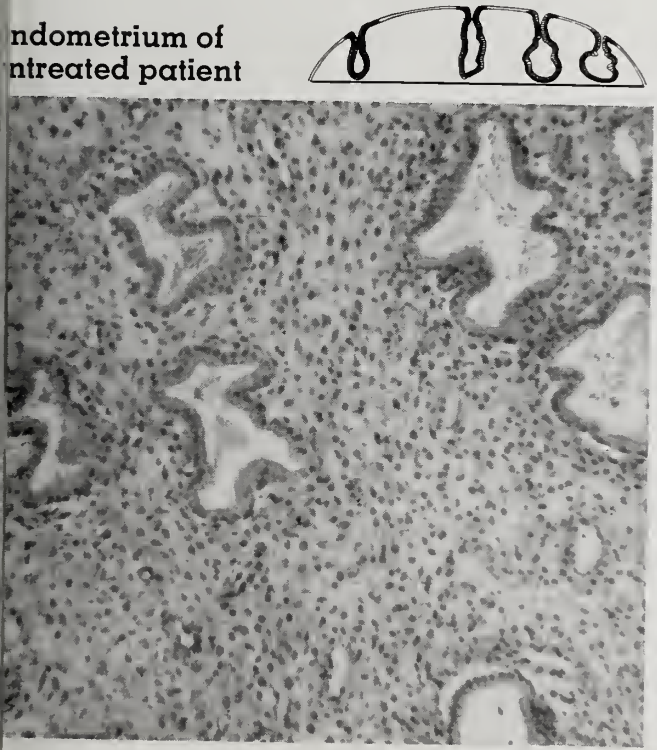


Immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

# How Norinyl-1 alters normal endometrial responses– another possible protective mechanism

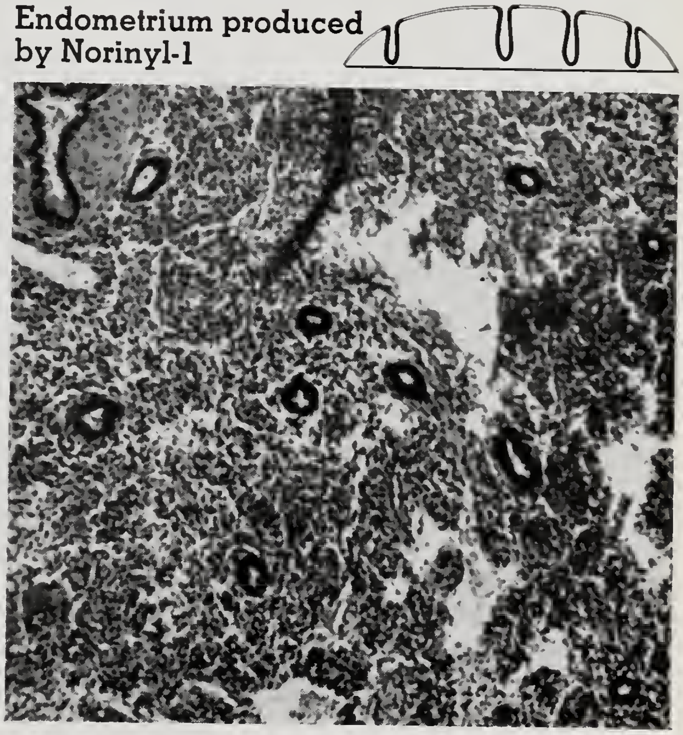
et us suppose that an ovum is released—as occurs in an ccasional, rare case—and somehow a sperm succeeds in enetrating the cervical mucus barrier. Should this come about, he additional action of Norinyl-1 may protect the patient om unwanted pregnancy. The theory is that progestogen intake akes endometrial tissue unreceptive to implantation.

**ndometrium of ntreated patient**



ormally, the endometrium progresses through proliferative phase stimulated by estrogen and a ecretory phase stimulated by progesterone. uring the secretory phase the endometrium is eceptive to the fertilized ovum.

**Endometrium produced by Norinyl-1**



When Norinyl-1 is administered its progestogen component—norethindrone—accelerates the secretory phase and suppresses glandular and vascular development.

new **Norinyl®-1** tablets

(norethindrone 1mg. $\bar{c}$ mestranol 0.05mg.)

e last page for contraindications, precautions, side effects and dosage.

effective fertility control
on half the previous dosage

maintains ratio
of the established
norethindrone/mestranol
combination

lower cost

new

# Norinyl-1®

(norethindrone 1mg. c̄ mestranol 0.05mg.) tablets

Reduction of oral contraceptive dosage to lowest effective levels has become a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now available in a new strength in which *both* norethindrone and mestranol are reduced 50 percent. Studies show that Norinyl-1 achieves fertility control with only 1.05 mg. of combined progestogen and estrogen per tablet.

Norethindrone was first reported for use as a progestational agent in human beings in 1955. Norethindrone 2 mg. with mestranol 0.1 mg., as an oral contraceptive, is currently in use by over 2,000,000 women. Clinical experience now establishes that Norinyl-1 also amply meets the criteria of reliability and safety.*

*Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965.

## PRESCRIBING INFORMATION

**Contraindications:** 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

**Warnings:** 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of Norinyl-1 in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

**Precautions:** 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with Norinyl-1. Therefore, if such tests are abnormal in a patient taking Norinyl-1, it is recommended that they be repeated after the drug has been withdrawn for 2 months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibroids may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac, or renal dysfunction, require careful observation. 5. Although a cause and effect relationship has not been established, Norinyl-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, as in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged Norinyl-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Norinyl-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. A cause and effect relationship has not been demonstrated. 11. Because of the effects of estrogens on epiphyseal closure, Norinyl-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask the onset of the climacteric. 13. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

**Side Effects:** The following adverse reactions have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma, breast changes (tenderness, enlargement and secretion), loss of scalp hair, change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, erythema multiforme, erythema nodosum, hemorrhagic eruption, migraine, rash (allergic), itching, rise in blood pressure in susceptible individuals, mental depression.

The following occurrences have been observed in users of oral contraceptives. A cause and effect relationship has not been established: thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory results may be altered by the use of oral contraceptives: increased bromsulphalein retention and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in $T^3$ values), metapyrone test, pregnanediol determination.

Other side effects reported to have occurred in association with use of this drug are dizziness, hirsutism, pains in legs, back, chest and abdomen, dysuria, drowsiness, vaginal discharge, libido increased and decreased, eruptions, hypermenorrhea, hypomenorrhea, increased appetite, G.U. infections, varicose veins, abdominal fullness, acne, headache, nervousness, allergies, blurred vision, pain in eyes, and itching in eyes. *For complete clinical data, see package insert.*

**Dosage and Administration:** 1. One tablet of Norinyl-1 is administered orally for 20 days beginning on day 5 of the menstrual cycle. (Count day 1 of the cycle as the first day of menstrual bleeding.) Repeat this dosage schedule for each cycle. 2. If no menstrual period occurs after a cycle of treatment (20 tablets) in which patient adhered to the schedule, the patient must be instructed to resume taking the Norinyl-1 tablets 7 days after the previous 20-day course was completed. For example, if the last pill of a previous cycle had been taken on a Sunday, then a new cycle of treatment should begin on the following Sunday. 3. In the postpartum woman, it is recommended that the first cycle of treatment should begin on day 5 of the first menstrual cycle. However, Norinyl-1 should not be administered during lactation.

**Availability:** Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.)—Dispensers of 20 and 60 and bottles of 250 tablets.

norethindrone — an original steroid from
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Photo professionally posed

# Mike expects a penicillin injection. He's about to be pleasantly surprised.

His physician is going to prescribe an oral penicillin —Pen•Vee® K (potassium phenoxymethyl penicillin). It's usually so rapidly and completely absorbed that therapeutic serum levels are produced in 15 to 30 minutes. Higher serum levels generally last longer than with oral penicillin G.

**Indications:** Infections susceptible to oral penicillin G: prophylaxis and treatment of streptococcal infections; treatment of pneumococcal, gonococcal, and susceptible staphylococcal infections; prophylaxis of rheumatic fever in patients with a previous history of the disease.

**Contraindications:** Infections caused by nonsusceptible organisms; history of penicillin sensitivity.

**Warnings:** Acute anaphylaxis (may prove fatal unless promptly controlled) is rare but more frequent in patients with previous penicillin sensitivity, bronchial asthma or other allergies. Resuscitative (epinephrine, aminophylline, pressor amines) and supportive (antihistamines, methylprednisolone sodium succinate) drugs should be readily available. Other rare hypersensitivity reactions include nephropathy, hemolytic anemia, leucopenia and thrombocytopenia. In suspected hypersensitivity, evaluation of renal and hematopoietic systems is recommended.

**Precautions:** In suspected staphylococcal infections, perform proper laboratory studies including sensitivity tests. If overgrowth of nonsusceptible organisms occurs (constant observation is essential), discontinue penicillin and take appropriate measures. Whenever allergic reactions occur, withdraw penicillin unless condition being treated is considered life threatening and amenable only to penicillin. Penicillin may delay or prevent appearance of primary syphilitic lesions. Gonorrhea patients suspected of concurrent syphilis should be tested serologically for at least 3 months. When lesions of primary syphilis are suspected, dark-field examination should precede use of penicillin. Treat beta-hemolytic streptococcal infections with full therapeutic dosage for at least 10 days to prevent rheumatic fever or glomerulonephritis. In staphylococcal infections, perform surgery as indicated.

**Adverse Reactions** (Penicillin has significant index of sensitization): Skin rashes, ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; serum sickness-like reactions, including chills, fever, edema, arthralgia and prostration. Severe and often fatal anaphylaxis has been reported (see "Warnings").

**Composition:** Tablets—125 mg. (200,000 units), 250 mg. (400,000 units), 500 mg. (800,000 units); Liquid—125 mg. (200,000 units) and 250 mg. (400,000 units) per 5 cc.

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**MEDICAL ANNALS**

*of the District of Columbia*

*September 1967* VOLUME XXXVI • NUMBER 9

## Wallace Mason Yater Number

At the request of many members, the Executive Board of the Medical Society of the District of Columbia is dedicating the September issue of the Medical Annals to Dr. Yater in recognition of 35 years of devoted editorial service. Dr. Stephen W. Nealon, Jr., who was appointed Guest Editor for this issue, secured the scientific papers which appear herein from physicians who were formerly Fellows at Georgetown University during Dr. Yater's tenure as Head of the Department of Medicine. Dr. John R. Cavanagh and Dr. J. Lawn Thompson, Jr., assisted Dr. Nealon in the planning of the Yater Number.

# Professor Wallace M. Yater—Some Recollections and Comments on His Contributions to Medicine*

THOMAS W. MATTINGLY, M.D., F.A.C.P.†

My first professional acquaintance with Professor Yater occurred in 1929 while I was a senior medical student at Georgetown University. On that occasion I was complimented before the entire class for having made what he considered an excellent case presentation and discussion of a patient with obstructive jaundice which had been assigned to me and selected by him for class discussion. Although I was surprised and embarrassed by his remarks, it was a pleasant occasion and in retrospect a profitable one. Two years later while a resident at Emergency Hospital he invited me to return to the University Hospital as a Fellow in Medicine. At that time, to my surprise, he made reference to my case presentations as a student.

Upon completing the year of fellowship, on his recommendation I spent an additional year in pathology instead of entering practice. During this second year in pathology I continued in medicine as an instructor and as an attending with a clinical service at both the University and Gallinger (now D. C. General) Hospitals. These were two very valuable years of training and experience and likewise very enjoyable ones. As a Fellow and young member of the staff in medicine, with Professor Yater as the only full-time member of the faculty, I was essentially in a preceptorship with all the opportunities of daily association and guidance.

In this brief presentation I shall enumerate some of the activities and observations of this professional association and training and offer a few comments as to Dr. Yater's contributions to medicine and to my career.

As a teacher, bedside clinician and diagnostician, I have never quite found his equal. His daily demonstration of the ability and the facility of obtaining the most as well as the critical information from the patient's history and physical examination and appropriately relating these to specific pathology and disease was unusual. He developed a highly competitive but coöperative spirit among his house staff and continually challenged them with problems and greater responsibilities. You became involved in a sort of

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* The reference numbers given in this paper are numbers from the list of Dr. Yater's publications which follows.

† Coördinator, Regional Medical Program of Metropolitan Washington, 2007 Eye Street, N.W., Washington, D. C. 20006.

"uppermanship" in which he took an active part. If you happened to come up with what was considered a brilliant diagnosis, you might receive credit for it, but at the same time you received a new and greater challenge. For example, in July 1932, shortly after beginning my fellowship, I recognized a case of Rocky Mountain spotted fever on the ward which was being treated as a septic abortion (fever, vaginal bleeding, and petechiae). I had had the opportunity of seeing 2 previous cases of Rocky Mountain spotted fever 1 and 2 years before. He accepted my suggestion but insisted that I substantiate my diagnosis. With the help and consultation of Drs. Dyer and Rumreich of the U.S. Public Health Service and because of rising titres of antibodies, the diagnosis was finally accepted. A second case of spotted fever was admitted in August 1932 for which he was sought as a consultant, and I in turn became a consultant to my chief. Credit was given, but a further challenge to my efforts was a notification from him (as editor of the MEDICAL ANNALS) that he had saved space in the September 1932 issue for a paper which I was to prepare on the Eastern type of Rocky Mountain spotted fever. This was my first attempt at medical writing, but I had no way of getting out of it.

He taught and stressed the importance of logic in diagnosis.[54] This logic had specific steps: (1) an accumulation of facts from the history and physical examination, (2) deductions made from this information, and (3) for a logical diagnosis there should be a heavy preponderance in favor of the diagnosis selected. He repeatedly cautioned against making a "snap diagnosis" and diagnosis from "hunches" or undue reliance on a laboratory test. You had to defend each and every laboratory test, both in practice and in the discussion of a particular case. A sure way to obtain his displeasure was to offer a diagnosis without a good reason for it. No credit was given for casual mention; a well written and precise note on the clinical record was necessary to receive consideration. I remember making rounds with him and his new intern staff on a hot July morning in 1933 and discussing the management of a heat stroke in a husky male who had been admitted the day prior with a temperature of 106° F. I went to the bedside and palpated an enlarged spleen and raised the question of the possibility of malaria instead of heat stroke. (I had recognized the patient, an ex-boxer from Mississippi who had been in Gallinger Hospital with recurrent malaria some months before.) Dr. Yater confirmed the finding of an enlarged spleen but ignored my suggestion with some disdain because he thought I was practicing "snap diagnosis." The malarial smear was positive, the chills and fever returned, and the patient was treated for malaria. I received no remarks or compliments from Dr. Yater for this diagnosis until some days later when in the quiet of his office he suddenly turned on me and asked, "How did you know that patient had malaria?" I knew that it had worried him. Like a kid caught with the stolen candy, I had to confess that I knew of his previous admission. I had learned another lesson in both diagnostic logic and professional behavior toward one's chief.

As a teacher, he never "spoon-fed" his students or Fellows. You were given what he thought was just enough information to provide a stimulus and he expected you to respond. I, like others who worked with him, soon found how to use the library. It was a mistake to mention a reference incorrectly or one of which one's knowledge or memory was vague. I am sure his insistence on correctness of references had some influence in the development of the encyclopedic memory and minds of Hugh Hussey and Sol Katz who worked with him in later years.

In 1933 I accompanied him to Walter Reed General Hospital where he had been asked to see a patient in consultation by Colonel S. U. Marietta, Chief of Medical Service (later Major General and Commanding Officer). This patient had a history of fever of a year's duration, great loss of weight, and back pain. A malignancy was suspected but could not be identified. A correct diagnosis was made of undulant fever with complicating vertebral involvement and paravertebral abscesses. This complication was not uncommon in southern France at that time. I reviewed and translated a number of these case reports from the French literature which received the attention and appreciation of General Marietta as well as Dr. Yater.

Following a few fortunate observations and diagnoses which I made in the cardiovascular field, an area of Dr. Yater's interest at that time, he interested me in working in the cardiac clinic with the late Dr. James Esler, a well-trained cardiologist who had come to Washington after studying in Philadelphia and Boston. While working there I had the occasion to recognize a coarctation of the aorta (a rare clinical diagnosis at that time) in a Negress who was being treated for hypertension and hyperthyroidism. Here again I found that I had been placed on the program of the Section of Internal Medicine of the Medical Society of the District of Columbia by Drs. Yater and Esler to present this interesting case and to discuss the clinical diagnosis of coarctation of the aorta. This presentation again attracted the attention of General Marietta who was present. He approached me after the program and invited me to join the staff at Walter Reed Hospital, promising to assign me to cardiology with Major Munley, a student of Sir Thomas Lewis and an outstanding cardiologist in the Army at that time. I accepted this invitation, entering active duty with assignment to Walter Reed, July 1, 1934. I entered the Regular Army Medical Service in October 1935.

Although Dr. Yater was responsible for my contacts and association with General Marietta, resulting in my entrance in the Army, he was very displeased with my decision. He feared that my professional career would be stifled in the Army and that I could do better elsewhere. Perhaps it was again the "challenge to prove him wrong" which stimulated me to greater effort in the military service. In later years when I returned to Washington after World War II, at which time Dr. Yater was in private practice and no longer the Professor at Georgetown, he again questioned my continuance in the Army. Later when I became Chief of Medicine and Cardiology at Walter Reed (the position held formerly by General Marietta) and upon promotion to Brigadier General, I received letters of congratulation from Dr. Yater. These letters had a greater meaning to me than many others as I realized that I had at last met his challenge of earlier years and these letters were evidence that his advice and predictions were not entirely correct.

The years 1932 to 1935 were important and busy years in Dr. Yater's professional career and a period when he made many of his important contributions to medicine. Only a few can be mentioned in this short discussion.

*Cardiovascular diseases.* Although he demonstrated a great interest in the broad field of internal medicine and physical diagnosis, it was quite obvious early in his career that the area of cardiovascular diseases constituted his greatest interest. Seventeen of the 28 publications he made prior to 1932 were related to this field. Directly and indirectly he fostered this interest in others who worked with him, including myself. Thus he brought the late Dr. Esler, a Boston-trained cardiologist and previous Fellow of Dr. Paul D. White, to the University staff at that time to head the Cardiology Clinic and to lecture and to teach electrocardiography in the Medical School. My additional association with and my greatest admiration for Dr. Esler, plus the stimulation from Dr. Yater, had much to do with my early interest as well as my continued interest in the field of cardiology.

Dr. Yater's interest in the cardiovascular area related specifically to clinical research, diagnosis, and pathology. I shall mention only some of the more important contributions in this field which occurred before, during and shortly after the period I spent with him.

*Disturbances of conduction, heart block.* He had perhaps the first case in which the diagnosis of complete heart block was made in the fetus in utero. He published an excellent review of congenital heart block early in 1929.[13] In 1932 and 1933, in association with Drs. McNabb and Cornell, pathologists of the old Army Medical Museum, he studied by serial sections the histopathology of the conduction system in several cases of congenital heart block in infants as well as heart block associated with congenital heart disease in the adult.[46, 60, 61, 72, 91, 93] I was the messenger boy in those early days who took the sections back and forth between the University Hospital and the Museum. As a reward I found opportunity to review these sections with the pathologist as well as to listen to and read the discussions of Dr. Yater and his associate pathologists. One of their cases of heart block was associated with calcareous lesions of the heart muscle.[65] This aroused my interest in calcification in the heart muscle and particularly that occurring within the heart valves. I collected a series of hearts from the pathology specimens stored in the attic in the Department of Pathology at the Medical School. In addition to studying the nature and location of the calcification in these hearts, with the help of Dr. Lawrence Otell, the radiologist at the University, we began to fluoroscope cardiac patients from the clinic with valvular heart disease, looking for calcification in the valve areas. We utilized the technique of Sosman of Peter Bent Brigham Hospital, Boston, who published several excellent papers on this subject at that time (Amer. J. Roentgen., 1933, **30,** 328). We likewise instituted the technique and study to determine the extent of calcification in the heart tissues, particularly valve areas, by taking X-ray films of autopsy specimens of the hearts (figure 1). Our interest at that time included calcification in the mitral annulus as associated with heart block and conduction disorders.

In recent years this subject of atrioventricular heart block associated with calcified mitral valve annulus and with aortic valve lesions has been revived with great interest. Likewise, interest in the calcification developed anew with the surgical approach to the treatment for congenital and acquired lesions. These earlier studies and investigations by Dr. Yater and his associates in the pathology of heart block formed the background for later studies by Lev, Manion and others who have made more extensive studies in recent years. Likewise, Dr. Yater's histopathologic studies of A-V block due to bilateral bundle-branch block[75] were the earliest confirmation of this mechanism of A-V block which again has seen recent revival of clinical interest.

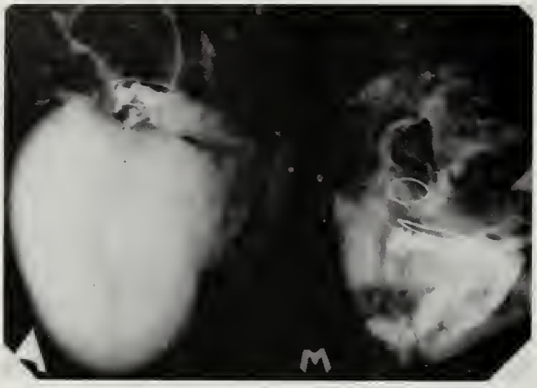

**FIG. 1. Roentgenograms of 2 hearts obtained from autopsy. Specimen on left is from a 48-year-old man with isolated severe aortic valve stenosis; specimen on right is from a 38-year-old woman with isolated tight mitral stenosis. Both were considered rheumatic in etiology. Metal wires were placed about the base of the mitral and aortic valves to aid in identification of valve areas. Calcification was identified in both patients by fluoroscopy prior to death in 1933.**

*Cardiovascular manifestations of hyperthyroidism (thyrotoxicosis) and the question of thyroid heart disease.* Because Dr. Yater was at the Mayo Clinic about the time that thyroxine was isolated from the thyroid gland and due to his interest in cardiovascular diseases, it was rather natural that he would have developed a clinical and investigative interest in this subject. In the laboratory he had earlier demonstrated the site of action of thyroxine in the perfused heart of the thyroxinized heart of rabbits.[32] The concepts as contained in publications in 1932 on the subject of mechanisms of adjustment of the circulation in hyperthyroidism,[38] the cause of heart failure in hyperthyroidism,[35] and given later in the Kober Lecture on "Goiter and the Heart" in 1938 have withstood subsequent years of basic and clinical research occurring since that early date. He pointed out that congestive failure rarely occurs with hyperthyroidism in the young individual with an otherwise healthy heart but occurs primarily in the middle-aged or elderly patient because of the effect of the metabolic abnormalities of hyperthyroidism on the heart, which is often the site of pathology from other etiologic factors. Likewise, myocardial hypertrophy, if it occurs in the young individual with hyperthyroidism, is slight in proportion to the increase in heart work by virtue of increased heart rate because the heart is working against a low peripheral resistance in the young with normal arterioles and capillaries which respond to the general vascular relaxation of hyperthyroidism.

*Experimental work in transplantation of the heart.* He became interested in the possibilities of transplantation of the heart and collaborated in experiments with Dr. Jacob Markowitz, first at the Mayo Clinic and later when the latter moved to the Department of Physiology at Georgetown in 1932. Working with Drs. Frank C. Mann and James T. Priestly of the Mayo Clinic, they succeeded in transplanting the heart of a puppy dog to the neck vessels of an adult dog.[44] This was likewise the beginning of worthwhile animal research in physiology and medicine at the University, soon to be followed by the addition of Dr. Theodore Koppanyi to the staff, who began animal research in pharmacology.

*Pericardial diseases.* In 1932 I had the occasion to see and follow up after a successful pericardectomy a patient with constrictive pericarditis who had been so diagnosed by Dr. Yater and a Fellow in Medicine, Dr. John Cavanagh, in 1931. This case, presented before the scientific meeting of the Medical Society of the District of Columbia by Dr. Cavanagh in May 1934, was referred to and included in subsequent publications of additional cases by Dr. Yater.[94, 109, 110] This was the first patient in the Washington area to have surgery for constrictive pericarditis. She was sent to Cleveland and became one of the earliest cases operated on by Dr. Claude Beck, pioneer heart surgeon. I was both fascinated and intrigued by the description of the surgical procedure and the high degree of tolerance of the heart to such a surgical procedure, as related by Dr. Cavanagh, who accompanied the patient to Cleveland and observed the surgery. This was the beginning of my interest in the potentialities of heart surgery which has existed through the years. Dr. Yater likewise collected a series of tumors and cysts of the pericardium as well as the heart and he made several publications on this subject,[24, 28] stressing both their symptoms and the diagnostic features.

*Systemic arterial hypertension.* Both primary and secondary forms of systemic arterial hypertension engaged the attention of Dr. Yater during this period. His concepts and teaching on this subject not only influenced those of us who were working closely with him but the practicing physicians in the Washington area as well. His earlier experience and publications with Drs. Keith and Wagener[6] at the Mayo Clinic, and Dr. Fahr at the University of Minnesota, gave him an unusual background and understanding of the diffuse nature and diverse effects of hypertensive arterial disease. As a medical resident on his service one was considered just "as naked" without an ophthalmoscope and sphygmomanometer as without a stethoscope. Likewise, you would never mention the possibilities of hypertensive disease without being prepared to give a detailed assessment, organ by organ, of the vascular symptoms, findings, and damage. As a reflection of this arousal of interest in the diagnosis of hypertensive vascular disease, 2 separate etiologic studies of heart disease about this time indicated that hypertensive vascular disease was the most common type of heart disease in Washington (Gager, L. T., and Dunn, W. L.: Med. Ann. D. C., 1932, **2**, 113), a fact which might be disputed, and its high incidence attributed to the unusual interest engendered at that time.[68] Several of his publications on this subject during those years remain excellent references and the concepts as enumerated remain firm[17, 36, 40]; however, one concept has not withstood the experience of time. In an editorial on the subject of essential hypertension in 1932[40] he stated, "All means of lowering the blood pressure by drugs are practically worthless," a statement which was true at that time, but which, fortunately, is untrue today.

*Arterial diseases.* In 1932 his presentation of a patient with congestive heart failure resulting from a traumatic A-V fistula and his demonstration of the features of the fistula, the pathologic alterations of the circulation, and later the removal of these abnormalities by surgery (Sanderson, F. R., and Murphy, W. S.: Med. Ann. D. C., 1932, **1**, 181) aroused my interest in the potentialities of traumatic heart disease. This was very profitable to me later in the military service and in publications on this subject in recent years. In February 1933, some months later, while at the old Gallinger Municipal Hospital as a Fellow in Medicine, I, along with Dr. Michael J. McInerney, the Medical Resident at the time, presented a 15-year-old youth with cardiomegaly and hypertension to Dr. Yater during rounds. We added as a surprise finding the presence of a traumatic A-V fistula and aneurysm as the probable cause of the cardiomegaly and hypertension and failure. He promptly challenged us to demonstrate the lesion by arteriography. Getting no response from us he proceeded to successfully inject Thorotrast® into the brachial artery with no equipment other than a 10 c.c. syringe, an ordinary needle, and a rubber tourniquet. The result was an excellent radiographic demonstration of the traumatic lesion, including the arteriovenous aneurysm (figure 2).[53] This to my knowledge was the first arteriogram performed in the Washington area. My participation was to release the tourniquet at the right time and to write the case report. In the subsequent years he or his collaborator, Dr. Otell, radiologist, published several articles on the utilization of Thorotrast in arteriography in the diagnosis of vascular lesions.[81, 82, 83]

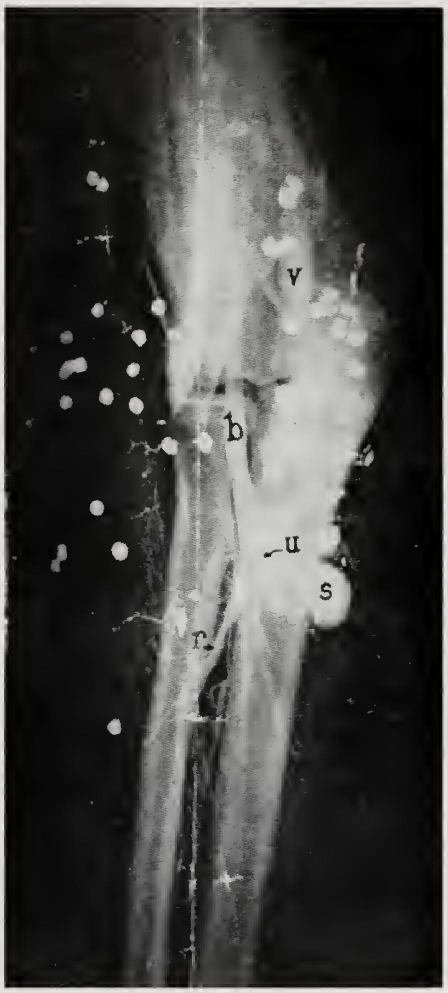

**FIG. 2. Roentgenogram of the right forearm with the palm upward. The numerous opaque spots are buckshot. b, Brachial artery; r, radial artery; u, origin of ulnar artery; s, sac of the arteriovenous aneurysm; v, vein draining the aneurysm.[53] Reproduced through the courtesy of Lea & Febiger, Philadelphia, Pa.**

[85, 87] With the discontinuance of the use of Thorotrast there was a large hiatus in which little progress was made in perfecting our present techniques of arteriography until during and after World War II. His pioneer work in this important field as we now know it is often forgotten by those who today master the highly sophisticated techniques and contrast studies in the diagnosis of cardiovascular diseases. In subsequent years he continued his interest in vascular lesions, publishing other papers on the subjects of traumatic and congenital arteriovenous fistula, mycotic arteriovenous fistula,[104] superior vena caval syndromes,[115, 130] and pulmonary arteriovenuous fistula,[137] as well as papers on the subject of ruptured arterial aneurysms,[97, 101] diseases of the aorta,[103] and diseases of arteries affecting the extremities.[85,111]

*Coronary artery disease.* I learned much from Dr. Yater regarding the wide spectrum of the pathology and manifestations of coronary disease. There was a general concept at that time (1932—34) that there was a low incidence of myocardial infarction in the Negro and that the disease of coronary atherosclerosis did not occur in young adults. He repeatedly pointed out that these concepts were erroneous and frequently presented illustrative cases to exemplify the exceptions. In the subsequent 10 years he made extensive studies and publications on coronary disease in young adults.[135] His detailed clinicopathologic study of coronary disease in young adults forms the basis for our increasing knowledge in this important area of coronary disease as we see it today.

*Research in rheumatic fever.* In 1932 Dr. Yater became very interested in the work of Dr. O. F. Hedley of the National Institute of Health in what was the beginning of research in heart disease by that Institute.* They began a bacteriologic study of rheumatic infections such as rheumatic fever, chorea, and active rheumatic carditis. Small amounts of blood from patients with these active diseases were subjected to various bacteriologic studies, including injection into monkeys. I obtained many specimens from patients at the University and Gallinger Hospitals during the period 1932–33. Great enthusiasm developed early in this study when some of these animals developed swollen joints suggesting the production of the disease in the injected animals, but it was soon appreciated that this was only hypersensitivity to the human sera. It is difficult to realize how such a modest beginning eventually led to the multimillion dollar research program of NIH today. The total initial appropriation for this new Institute of Scientific Research for the U. S. Public Health Service, created by legislation in 1930 with a stated function to ascertain the cause, prevention and cure of disease affecting human beings, was $750,000, which was expended primarily in construction of the first 2 buildings.

*Diagnosis of diseases of the liver and spleen (hepatosplenography).* The diagnosis of diseases involving these organs always intrigued Dr. Yater. When I was very ill with typhoid fever in 1933, Dr. Yater, with Dr. John Minor, my physician, came to see me. I was sure he was going to palpate my spleen. I was not disappointed that he did so and that he took the occasion to demonstrate his finding to others present.

Early in 1931, following the initial work and publications of Radt et al of Germany (Klin. Wchnschr., 1929, **8,** 2128), he became interested in a method of visualization of the liver and spleen after the intravenous injection of thorium dioxide sol (Thorotrast), a substance of high atomic weight which is phagocytized by the reticulo-endothelial cells of the body. He was the first physician in the United States to use this technique and contributed the first publications to the English literature on the subject. I had the occasion to see most of the first of the hundred or more patients studied with this diagnostic technique, as was reported by Drs. Yater and Otell in 1933.[50] The diagnostic value of this procedure proved to be of great help in many liver diseases,[52, 80, 86] but it became unpopular and was later questioned as a safe procedure in clinical medicine because of the potentialities of latent radioactivity and the potential carcinogenic activity of the Thorotrast which was retained in the tissues. However, this was the beginning of our present-day armamentarium of isotope-scanning techniques which we find very valuable in diagnosis.

*Contributions to medical education, to Medical Society activities, to medical socioeconomics.* During this period Dr. Yater was extensively engaged in many professional activities outside the Medical School and University Hospital in a variety of ways. He encouraged his Fellows and young staff members to do the same, often using the technique of committing them to a scientific program or other activity and informing them after they had been scheduled. At that time he was Governor for the District of Columbia of the American College of Physicians. I attended my first annual session of the College in Washington, D. C. in March 1931 at his suggestion. He likewise introduced me to many of the officials of the College during the annual session in Philadelphia in 1935, thus furthering my interest in this organization. He was active in the formation of the Washington Heart Association and was chairman or member of many committees of the Medical Society of the District of Columbia. While he was a member of the Committee on Public Relations of that Society, the Committee wisely recommended having a full-time executive secretary. He likewise was chairman of a committee for coördination of the resources for medical care, and along with Ross Garrett developed plans for a Medical-Dental Service Bureau; he was Chairman of the Board of Directors of the latter in 1935.

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* NIH studies on rheumatic fever. Med. Ann. D. C., 1932, 1, 304 and 326.

He engaged in many other activities in an effort to solve the many problems as seen in medicine at that time. About 1932 the country was also interested, as today, in the cost of medical care, and at that time President Hoover appointed a committee (the Wickersham-Wilbur Committee), which presented findings and recommendations that went unheeded, probably because the recovery from the ensuing depression which occurred in the following years took care of many of the problems. A comment from an editorial in the MEDICAL ANNALS, "Concerning Costs of Medical Care and Attempts at the Socialization of Medicine" by Dr. Thomas A. Groover ( November 1932, page 327), sounds much like the theme of President Johnson's recent committee on heart, stroke and cancer of today: "It may be said that medical progress and the means for adequate distribution of its admitted benefits are out of step." Dr. Yater became very much interested in these problems, and he was one of the pioneers in the discussion of socioeconomic problems in medicine of that time, using the MEDICAL ANNALS for appropriate editorials and discussions. He established the first course in medical socioeconomics in any medical school curriculum at Georgetown.

*Continued medical education and scientific publications in the Journal of the D. C. Medical Society.* Perhaps Dr. Yater's greatest contribution at that time, besides that of his academic activities at the Medical School, was as Editor of the MEDICAL ANNALS, which he began in January 1932. He and his committee outlined the scope and objectives of this new journal in the initial January issue.[29] He firmly resolved that this new journal would remain a substantial professional journal and not degenerate into a simple publication of the activities of the Society as had the *Bulletin*, its predecessor (1924–1932), but that it would be a revival of the *Washington Medical Annals* as published during the period 1901 to 1920 under the able editorial management of the late Dr. Daniel S. Lamb. Dr. Yater actively sought scientific publications from members of the Society, many of the type which had been published in other national journals, and stimulated others to prepare new material for publication; at the same time he insisted on quality in his publication. During the first 2 years he contributed a number of editorials on current subjects, some of which are excellent analyses of educational and professional problems of that time and have application to the present. In an editorial submitted, "Future of Washington as a Medical Center,"[33] he presented logically why Washington should be a medical center, pointing out reasons why it had not developed into a center and offering recommendations for progress in this area. In another editorial in 1934[63] he stressed the difficulties in keeping up with medical literature, a problem that is even worse today. He stressed "active teaching and contact with the young graduate house staff as a means of keeping current." Again, in an editorial in 1933,[57] entitled "The Practitioner's Scientific Betterment," he stressed the importance of selectivity in medical literature and made a plea for attendance and participation in local and national scientific meetings. As a means of assisting in continuing medical education for physicians in the Washington area he began the preparation and publication in the November 1933 issue of a series of articles on subjects concerned with the everyday practice of medicine. His first series,[58] which was on his favorite subject of heart disease, continued until June of 1934.

In the 35 years of his activities and interest with the ANNALS, he has continued to maintain the scope and objectives as outlined in the first issue in January 1932. Few people can make such a resolve and keep to it so well. It is indeed an example which his associates have found difficult to follow.

I have spent considerable time enumerating the many contributions Dr. Yater has made, including ways in which he contributed to the subsequent careers of his Fellows. I find it very difficult to think of any small contribution by which I, as one of his Fellows, have in any way affected his career. Dr. Louis Garcia, a fellow associate with me in 1932–33, and I have always insisted that we were responsible for getting our bachelor professor married in 1932. We believe that Millicent was the best thing that ever happened to our Chief (see page 550) and would like to take some credit for this great success in his career.

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# A System of Continuing Medical Education

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It is an honor to contribute to this *Festschrift* dedicated to Wallace M. Yater, Professor Emeritus of Medicine, Georgetown University School of Medicine, and my friend. Dr. Yater is a great teacher. Through his extraordinary service to the Medical Annals of the District of Columbia and the American College of Physicians he has shown himself a powerful protagonist of organized continuing medical education. (The editor of a medical journal leads an organization dedicated to constant reëvaluation and improvement of the practice of medicine.) And so, the occasion seems appropriate for describing experiences in continuing medical education and developing some thoughts on organizing medical education into an efficient system.

The public is increasingly concerned with the inner workings of medicine—new scientific advances, both basic and clinical, socioeconomic considerations, the distribution of medical services and personnel, and the professional competence of physicians. There are distant murmurs of relicensing and recertification of practicing physicians. These ideas could be very attractive to the public—our patients—and legislators, if there were not clearly discernible efforts on the parts of all individual physicians and the profession as a whole to keep operational medicine scientifically current, everywhere and at all times.

Regional requirements differ in the field of continuing medical education. The Washington Metropolitan Area is a highly sophisticated medical community. Here we have 3 medical schools, an outstanding State Medical Society, several modern and well-equipped community hospitals, including the leading medical facilities of the military services, the National Library of Medicine, National Institutes of Health, and so on. Lectures, courses and conferences are held every day. Every day there is something for every physician.

Many, many of our physicians partake liberally of the educational buffet. Specialty groups meet frequently. Some of the weekly conferences in our medical schools attract large numbers of practicing physicians. Many physicians also have regular reading programs which they follow conscientiously. New audiovisual devices facilitate the task for some.

On the other hand, there are busy physicians whose educational diets are inadequate even in the midst of surplus. The analogy to nutritional deficiency in an affluent society is tempting. The problem can be psychologic, as in anorexia nervosa (lack of motivation); dietary intake can be unbalanced due to faddism (plenty of meetings but few scientific ones); there may be an absorption defect due to lack of an essential enzyme (poor habits of study); or tissue utilization of essential foodstuffs may be defective because of degenerative disease (fatigue, poor attention span).

Under some conditions of clinical practice opportunities may truly be lacking, such as in smaller communities that are off the beaten path. However, most physicians work at a hospital where there is an opportunity to meet and exchange information and discuss clinical problems with other physicians. The usual hospital-based physicians—the pathologist, the radiologist, occasionally the director of medical education (DME)—frequently provide the focal point for an informal continuing educational program.

In communities such as Washington the specialty groups will continue to meet regularly, organizations (American College of Physicians, American Heart Association, etc.) will continue to sponsor courses, and the conferences at the medical schools will go on. The continuing educational menu will be varied and the fare delicious and nicely served. But everyone isn't at the table, and the dinner hours are irregular.

This brief essay proposes a system of continuing education in which the medical school faculties are the teachers, the community hospitals are the classrooms, and the hospital staffs are the classes. The proposal is based on long experiences of Georgetown University School of Medicine with affiliated hospitals in New York and Massachusetts and recent experiences with a continuing education program at Providence Hospital in Washington.

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Universal applicability of the principles described depends on acceptance of the view that the best teachers of medical science are the workers in the fields, the investigators who bring current biochemical and physiologic thinking to the teaching exercise in the classroom or at the bedside. Further, acceptance is required of the view that all physicians, regardless of specialty interest or type of practice, need periodic review and discussion of those areas of basic science and clinical medicine in which significant advances are being made. Finally, the purpose of the whole system requires emphasis over and over again, for it gives meaning to what can sound like a dull exercise. The primary objective of continuing medical education is the improvement of the quality of medical practice everywhere.

### University-Voluntary Hospital Relationships

Relationships exist between medical schools and voluntary community hospitals for varying purposes. From the medical school's viewpoint one purpose is the furthering of the school's undergraduate and house-staff training programs. In the minds of many medical educators, and certainly in Georgetown's view, a voluntary community hospital in the complex of teaching hospitals, under firm and comprehensive articles of affiliation, is a valuable asset. Georgetown has had such a relationship with Arlington Community Hospital for many years. New relationships of this type are developing. No one can question that this kind of relationship elevates standards of patient care in the community hospital. However, medical school resources are limited, and relatively few community hospitals can develop an affiliation for training programs.

In the early 1950's Dr. Harold Jeghers, then Professor of Medicine at Georgetown, was the prime mover in an experimental program of affiliation with 4 distant voluntary community hospitals: St. Mary's Hospital, Rochester, New York; Mercy Hospital, Buffalo; Kenmore Mercy, Kenmore, New York; and St. Vincent Hospital, Worcester, Massachusetts. These affiliations were based on "the decision to explore what could be accomplished by bringing postgraduate education to a non-university hospital rather than conducting some postgraduate courses at the university center."[1]

Details of these affiliations have been elaborated elsewhere.[1, 2] Members of Georgetown's faculty have visited the hospitals on a regular rotating basis. They spend a day or two at the hospital conducting ward rounds and giving conferences to the attending physicians and house staff. The objective, again, is the improvement of patient care in these hospitals. While this is a worthy objective, evaluation of the effectiveness of the program has been extremely difficult.

From the outset administrators and physicians of affiliated hospitals were pleased with the program. Unfortunately, a primary reason seemed to be the possibility of attracting more and better house staff. All agreed that the quality of patient care was upgraded.

Reactions of the faculty of the School have not been uniformly favorable. Some feel that unreasonable demands have been made on their time. They feel that more can be accomplished by other techniques and that the conduct of continuing educational programs at the University itself is more fruitful.

It should be emphasized that one of the important objectives of a medical school is continuing education. Some medical school faculties are well aware of their obligations in this regard. This is particularly so in state universities in which the faculty has a legislated mandate in the field of continuing education. This objective is frequently not stressed in medical schools, and this is the fault of school administration. Considerable effort on the part of deans and department chairmen is required to sustain this type of program, maintain enthusiasm in the faculty, and develop coöperation of basic scientists and clinicians in all areas of medicine in balanced proportions. Perhaps the strongest element in sustaining our distant affiliated hospital program for 16 years has been the awareness that we have been engaged in an experiment in medical education. Discouragement has resulted only from the inability to develop specific methods of evaluation and recognizable phases to the program.

In each of the cities where affiliated hospitals were located there were nearby medical schools. In discussions of the Education Committee of Georgetown University School of Medicine it was thought that the outcome of these programs should be the development of the hospitals to the extent that they would become desirable affiliations for the regional medical schools. In the case of St. Mary's Hospital in Rochester that endpoint was reached with the affiliation of St. Mary's with the University of Rochester on July 1, 1966.

Objectively, it would appear that brief periods spent in the environment of the community hospitals are of value to full-time academic physicians. In turn, the participation of physicians engaged in research brings advanced knowledge and new information directly to the practicing physicians of the hospitals. The faculty visits have played an important role in attracting competent staff to the hospitals. After the initial years, and except for the first year when a new director of medical education has reported, housestaff recruitment has probably not been significantly enhanced.

By virtue of our experiences in distant affiliated community hospitals, and especially because of decreasing commitments to these hospitals, discussions were held, early in 1965, with representatives of community hospitals in the Washington Metropolitan Area concerning programs of continuing medical education for their staffs. This resulted in the inauguration, in September 1966, of an affiliation with Providence Hospital. The Providence Hospital affiliation was patterned after the distant affiliations in New York and Massachusetts. Members of the faculty of the School of Medicine visit weekly at Providence, providing a basic science lecture and discussion, and biweekly to participate in clinical ward rounds.

The reception of this program by the hospital staff has been enthusiastic. The basic science lectures and discussions have formed a course, "Pathophysiology of Disease," which has progressed to a more clinically oriented program in the second year. Participation in biweekly "grand rounds" has been rotated among the clinical departments and has followed the general pattern of such conferences in university medical centers.

Hospital administration, again, has been extremely coöperative, responding to the expressed needs of hospital staff for continuing educational programs. Attendance by physicians and house staff has exceeded expectations and has proved stimulating to the majority of medical school faculty involved. The saving of time spent in travel and nights away from home has, in part, pleased those members of the faculty who had developed a negative attitude with regard to the distant affiliations.

Discussions are under way at this writing that will expand a modification of this program to Holy Cross Hospital, Silver Spring, Maryland. A pattern is now discernible that provides the template for a working system of continuing medical education with almost universal applicability.

## A Regional Plan

Continuing medical education is an important element in the Regional Medical Programs, as described in this journal by Mattingly.[3] In a sense it is unfortunate that the categorical "heart disease-cancer-stroke" label sticks to the Regional Medical Programs, because the overall need for regional coöperative endeavors in all areas of medicine is quite evident. The continuing educational plan that can be developed from the school-hospital relationships that I have described applies to any region that contains 1 or more medical schools, whether in categorical programs or not.

Shannon[4] has proposed that every sixth year of a practicing physician's career should be spent in a formal education process. While returning to a university for a year would provide a very profitable experience for the practicing physician, facilities at the university now appear too limited for application of this program on a large scale. The physical facilities, the patients for teaching, and the students themselves are available in the private non-university community hospitals. Indeed, in the community hospital setting there is, in addition, an element of persuasion—a veritable truant officer.

The outline of the plan is simple. Each accredited voluntary community hospital of certain characteristics (number of physicians, number of beds) must be affiliated with a medical school for the purpose of continuing medical education of the hospital staff. The school should be nearby, but, of course, this is not always possible. The medical schools of a region, or a city, should share this responsibility to the community or region.

The hospitals should pay costs of the program.

Conferences should be conducted on at least a weekly basis, and attendance by the hospital staff should be semi-obligatory. There should be a continuing emphasis on basic science as applied to clinical medicine. While the highly specialized groups should continue to meet for discussions of cases and developments in their fields, all physicians should attend a conference on developments in the broad fields of medicine and surgery.

A medical director, or director of medical education, or other designee of the hospital should meet on a regular basis with an associate dean or other designee of the school for planning of the program and evaluation. Hospital and school administrators must meet regularly. All steps must be taken to maintain a continuing sense of obligation among faculty and among hospital staff members. The talents of the school must be available to the hospital for consultation in matters of medical education. Care must be exercised that goals are not confused. The objectives of the program are not enhanced recruitment of house staff or the development of an affiliation for school training programs.

### Final Comments

Courses at distant places, or the great annual meetings of our societies and associations (American Medical Association, American Academy of General Practice, American College of Surgeons, American College of Physicians, etc.) are magnificent educational episodes. They are important and useful annual excursions, but they are not part of the practicing physician's way of life. The plan sketched briefly and roughly in these pages provides a built-in program for every physician. It has universal applicability and contains a freedom and flexibility that makes it locally adaptable and subject to the control of the regional practicing physicians.

Implementation of this system on a broad scale will sometimes require painful revisions of attitudes, both among medical school faculty and the community of practicing physicians. On the other hand, the purpose of describing Georgetown's experiences with distant and regional affiliations for continuing education is to indicate that this system can work.

Continuing medical education is a popular subject these days. It is being discussed by those who neither teach nor practice medicine. Our profession must take the lead in developing effective continuing educational programs and seeing to it that all physicians keep up to date.

Acknowledgments: Among those who have contributed creatively to the principles and events described in this paper, the following are preëminent: Dr. Harold Jeghers, now Medical Director, St. Vincent Hospital, Worcester, and Professor of Medicine, Tufts University, School of Medicine; Dr. Hugh H. Hussey, formerly Dean, Georgetown University School of Medicine, now Director of Scientific Activities, American Medical Association; Dr. John J. Butler, formerly Director of Medical Education, St. Mary's Hospital, Rochester, now Director of Medical Affairs, Catholic Medical Center, Brooklyn; Dr. John O'Brien, Director of Medical Education, Mercy Hospital, Buffalo; Dr. John F. Stapleton, formerly Director of Medical Education, St. Vincent Hospital, Worcester, now Associate Dean, Georgetown University School of Medicine; Dr. Bruce I. Shnider, Associate Dean, Georgetown; Dr. Laurence H. Kyle, Professor of Medicine, Georgetown; Dr. Robert J. Coffey, Professor of Surgery, Georgetown; Dr. Thomas Curtin, Medical Director for Staff Education, Providence Hospital; and Dr. William D. Dolan, Chief, Pathology Service, Arlington Community Hospital.

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# Atrial Pulsation of the Chest Wall*

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PALPABLE MOVEMENT of the precordium has been extensively studied in recent years with various techniques of recording. Abnormal chest-wall pulsation during systole has been widely recognized to be related to enlargement of 1 or both ventricles. Although diastolic movement of the chest wall has not been as thoroughly analyzed, several recent reports[1, 2, 3] have called attention to presystolic pulsation of the chest wall, attributing this movement to forward thrust of the ventricles during atrial systole.

In the course of studying chest-wall movement in a variety of diseases a number of patients have been encountered in whom the major or only palpable movement occurred during atrial systole. This report reviews 7 representative cases with special reference to chest-wall pulsation during atrial systole.

## Material and Methods

Chest movement was recorded by the system introduced by Eddleman and co-workers[4] known as kinetocardiography. This technique employs a flexible metal bellows probe held to the chest wall by externally supported clamps. The probe is a slender metal rod which can be placed for precise localization of pulsations. As the probe and bellows move with the chest wall, changes in air pressure within the bellows are converted by a Statham PM5 transducer into electrical current which can be introduced into any standard recording system. The recordings in this study were made with a Sanborn Poly-Viso recorder or an Electronics for Medicine photographic recorder or with the Sanborn Twin Beam phonocardiograph. In the latter instance the transducer output was introduced into a Sanborn strain-gage carrier preamplifier whence the signal was passed into the DC input of the Twin Beam ECG amplifier.

Following the nomenclature of Eddleman et al,[4] recording positions of the chest wall were designated with the letter K and a subscript numeral identical to that used in designating electrocardiographic V lead electrode positions. With this recording system, upward deflection represents outward movement and downward deflection, inward movement.

The 7 cases reported below were examined within a 6-month period on the medical service of the Landis State Hospital or of the Hospital of the Woman's Medical College of Pennsylvania.

## Report of Cases

**Case 1.** J. C., a 33-year-old Negro woman, was admitted for evaluation of recurrent attacks of paroxysmal tachycardia for 13 years associated with dizziness and chest pain. She had no cardiovascular symptoms between attacks. At the age of 20 she was told that her heart was enlarged.

The blood pressure was 130/80. A diffuse lift of the lower precordium was palpated with maximum thrust at the apex. Atrial and ventricular filling sounds were present as well as a grade II pulmonary ejection systolic murmur. ECG disclosed abnormally broad, peaked P waves and inverted T waves in $V_1$ through $V_5$. Chest X-ray films revealed diffuse cardiac enlargement. The patient was thought to have primary myocardial disease. A kinetocardiogram (figure 1) disclosed a striking presystolic movement (A) at $K_4$ (PMI).

**Case 2.** J. R., a 70-year-old white man with diabetes mellitis and chronic, far-advanced pulmonary tuberculosis, was hospitalized for treatment of active tuberculosis. Bilateral pleural plombage had been previously accomplished. He had suffered paroxysmal rapid heart action for several years in the past and had received digitalis therapy. Dyspnea on slight effort was attributed to his lung disease. The blood pressure was normal. No cardiomegaly or abnormal auscultatory findings were elicited. Palpation disclosed a mild but definite lower sternal and left parasternal lift followed by retraction. Simultaneous auscultation and palpation indicated the lift to be presystolic and the retraction to be systolic. This was confirmed by the kinetocardiogram which was recorded simultaneously with the right ventricular pressure pulse at cardiac catheterization (figure 2). An ECG exhibited complete right bundle-branch block. A chest X-ray film disclosed

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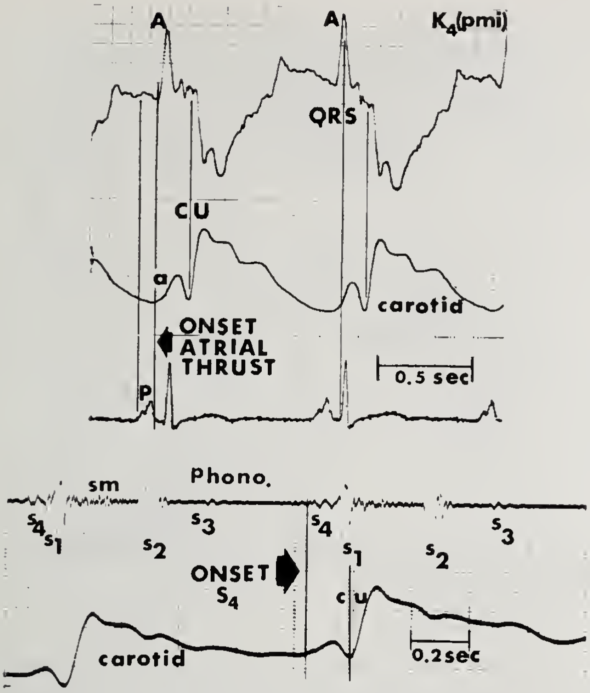

**FIG. 1. Apical impulse in a 34-year-old woman with primary myocardial disease (case 1). Prominent presytolic thrust (A) commences during descending limb of electrocardiographic P. a—Atrial deflection of carotid pulse. Phonocardiogram (bottom panel) exhibits atrial amd ventricular filling sounds. The atrial sound ($S_4$) begins 0.15 sec. prior to carotid upstroke, the time of peak presystolic movement. CU—carotid upstroke, $S_3$—ventricular filling sound, $S_4$—atrial sound.**

bilateral apical plombage with pulmonary retraction and fibrosis. The cardiac silhouette was distorted by the deformed lung architecture but was not grossly enlarged. Pulmonary and right ventricular hypertension were demonstrated during cardiac catheterization. The patient was considered to have moderately advanced cor pulmonale.

**Case 3.** A. W., a 75-year-old Negro woman with mild diabetes mellitus, was admitted with an acute anterolateral myocardial infarction and mild congestive heart failure. Examination disclosed mild cervical venous engorgement, scattered basal inspiratory rales,

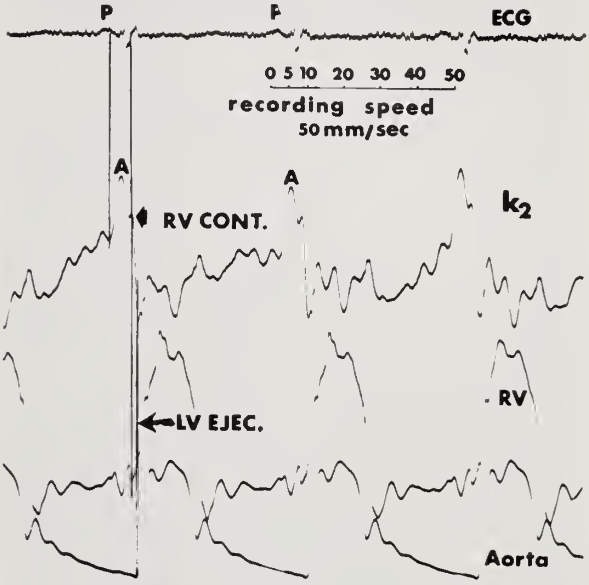

**FIG. 2. Lower, left parasternal movement in a 70-year-old man with cor pulmonale (case 2). Presystolic thrust (A) precedes ventricular contraction as depicted by simultaneous aortic and right ventricular pressure pulses. This movement was correctly timed by palpation prior to kinetocardiography. Pressure pulses were recorded at different sensitivities.**

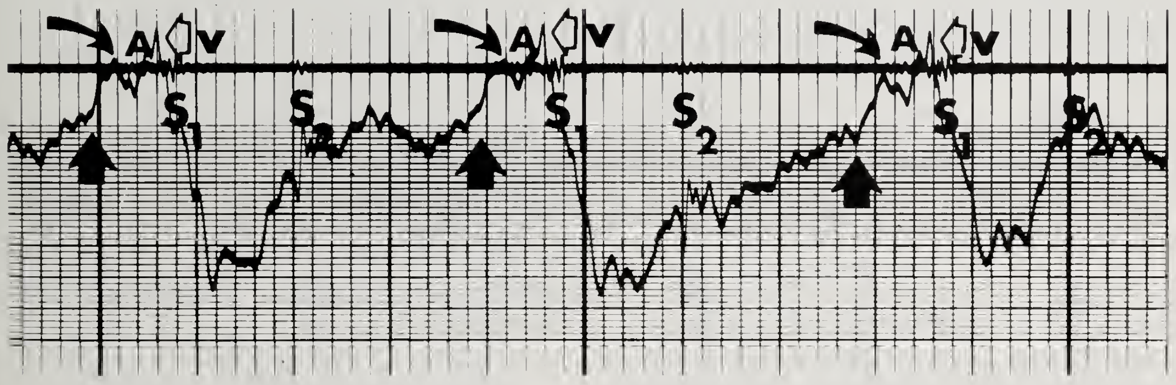

**FIG. 3. Lower, left parasternal movement in acute myocardial infarction (case 3), which was palpated as a vigorous thrust and thought to represent a systolic "bulge" until the kinetocardiogram disclosed the impulse to be presystolic. Heavy arrow designates onset of outward chest-wall movement coincident with atrial contraction. Note that atrial gallop sound (A) commences at peak of atrial thrust (curved arrow). Descending limb of atrial movement interrupted by outward movement of early ventricular contraction (V-open arrow), further prolonging the total outward movement, which then ceases abruptly with onset of first heart sound ($S_1$). Recording speed 75 mm./sec., time lines 0.04 sec.**

soft atrial gallop rhythm, and multiple ventricular extrasystoles. A barely perceptible diffuse precordial movement was evident upon careful palpation. By the third hospital day the atrial gallop had become notably louder, and precordial movement was palpated as a diffuse, vigorous thrust, maximum in the lower left parasternal region but extending to the apex. Initially this thrust was interpreted as the systolic "bulge" of myocardial infarction, but a kinetocardiogram (figure 3) disclosed the principal outward movement to be presystolic. An ECG exhibited the typical pattern of acute myocardial infarction. Chest X-ray films disclosed slight cardiomegaly.

**Case 4.** L. F., a 38-year-old obese Negro woman, was admitted for severe dependent edema. Examination disclosed acute pharyngitis and tonsillitis. The blood pressure was normal. The cervical veins were distended at 45°. A nodular goiter was palpated. The lungs were clear. Sinus tachycardia was present with a loud atrial gallop and a grade II apical systolic murmur. Palpation disclosed a brisk lower left parasternal and xyphoid pulsation. The movement was easily recognized to be a bifid or double impulse. A kinetocardiogram depicted the principal movement to correspond to atrial contraction (figure 4), coinciding with the atrial gallop (figure 5). A second major outward thrust commenced 0.06 second prior to the carotid dicrotic incisura. An ECG exhibited marked left axis deviation with prominent peaked P waves. Chest X-ray films revealed moderate diffuse cardiomegaly. A throat culture grew normal bacterial flora.

This patient exhibited chemical evidence of hyperthyroidism and responded well to therapy for hyperthyroidism and congestive heart failure. The cause of her cardiac disease was not established with certainty. It was thought likely that underlying myocardiopathy explained the severe cardiac failure which seemed disproportionate to the degree of hyperthyroidism. The possibility of myocarditis related to viral infection was considered but not proved.

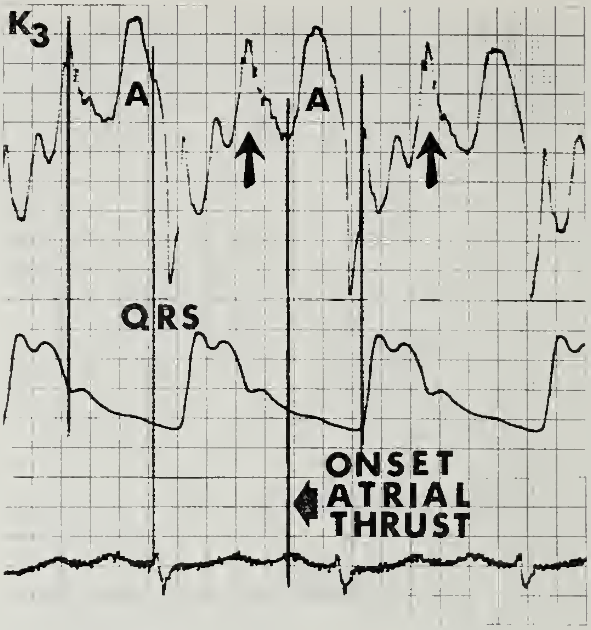

**FIG. 4. Lower, left parasternal movement in a 38-year-old woman with hyperthyroidism and possible primary myocardial disease (case 4). A double movement could be felt on palpation. Note that larger impulse (A) is presystolic, commencing with peak of the electrocardiographic P. The second thrust (arrow) occurs during early ventricular relaxation and may represent ascent of the A-V septa with vigorous atrial filling. Recording at 50 mm./sec., time lines 0.02 sec.**

**Case 5.** J. Q., a 43-year-old white man with previously diagnosed but asymptomatic rheumatic heart disease, was hospitalized for a functional gastrointestinal disorder. Examination revealed an anxious, normotensive man with normal cervical vessels. Regular sinus rhythm was present. The first heart sound was accentuated, and the second sound was normal. A loud mitral opening snap initiated a grade II diastolic

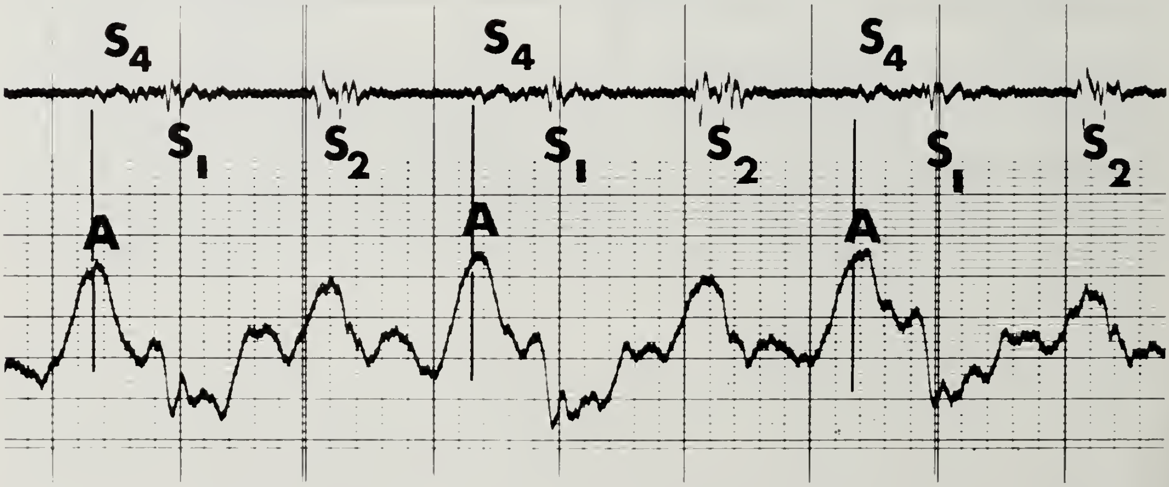

**FIG. 5. Same kinetocardiogram as in fig. 4, recorded at 75 mm./sec. with phonocardiogram. Microphone at lower, left sternal edge. Note onset of atrial gallop sound ($S_4$) at peak of atrial thrust (A).**

rumble with presystolic accentuation. Palpation demonstrated a quick, forceful outward movement of the lower left chest wall extending from xyphoid to apex, which a kinetocardiogram revealed to be presystolic (figure 6). An ECG disclosed slight right axis deviation and P mitrale. Chest X-ray films depicted a normal cardiac silhouette.

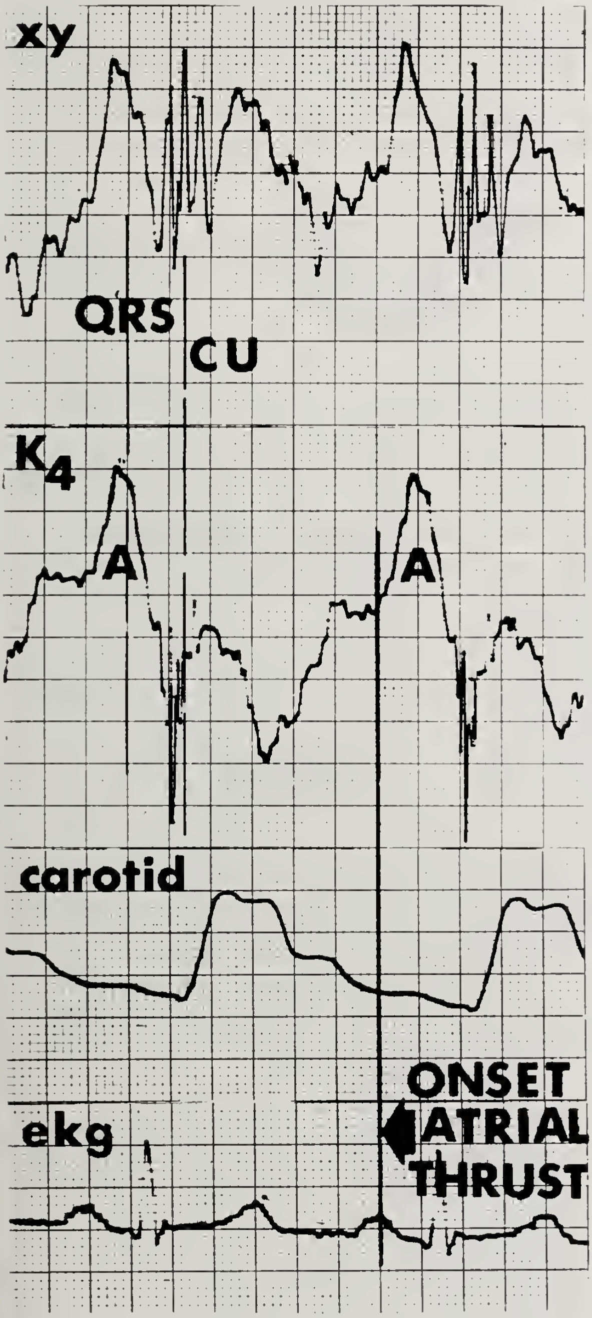

**FIG. 6. Xyphoid and apical movement tracing of a 43-year-old man with mitral stenosis (case 5). A readily palpable lift was felt across the precordium. Recordings disclosed the impulse (A) to be presystolic, commencing with the descending limb of the electrocardiographic P wave. CU—carotid upstroke. Recording at 50 mm./sec., time lines 0.02 sec.**

**Case 6.** H. P., a 63-year-old hypertensive Negro, was admitted with acute pulmonary edema of sudden onset. He had been in good health except for occasional angina pectoris in recent years. He became asymptomatic promptly with therapy. Examination disclosed regular sinus rhythm with normal heart sounds and no murmurs. A diffuse lower left parasternal movement was palpated from the sternal edge to the apex. Kinetocardiogram disclosed this movement to be presystolic and to be maximum at $K_2$ (figure 7). ECG exhibited left ventricular hypertrophy, and a chest X-ray film prior to discharge revealed a normal cardiac silhouette.

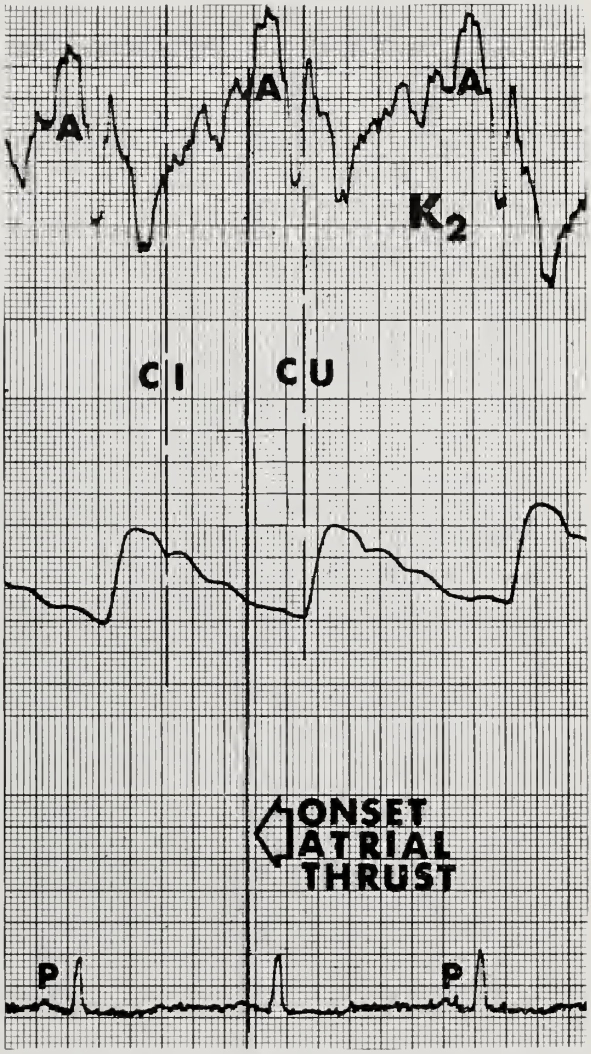

**FIG. 7. Precordial movement of a 63-year-old man with hypertension and coronary heart disease (case 6). Diffuse lower, left parasternal impulse is seen in $K_2$ recording to be presystolic, commencing just after the peak of ECG P wave. CU—carotid upstroke. CI—carotid incisura. Recording at 50 mm./sec., time lines 0.02 sec.**

**Case 7.** W. J., a 38-year-old man, was admitted for cardiac evaluation because of exertional dyspnea. He had rheumatic fever at the age of 17. The blood pressure was 140/20, and there were bounding, bisferiens peripheral and carotid pulses. A diffuse, vigorous precordial impulse was palpated from sternum to apex. Simultaneous auscultation and palpation disclosed this movement to be presystolic. A harsh grade III aortic systolic ejection murmur and a grade IV blowing aortic diastolic murmur were auscultated at the cardiac base. A grade II apical diastolic rumble with presystolic accentuation commenced with a third sound in early diastole. The first sound was softened, and the second sound was normal. An ECG and an X-ray film of the chest disclosed moderate left ventricular and left atrial enlargement.

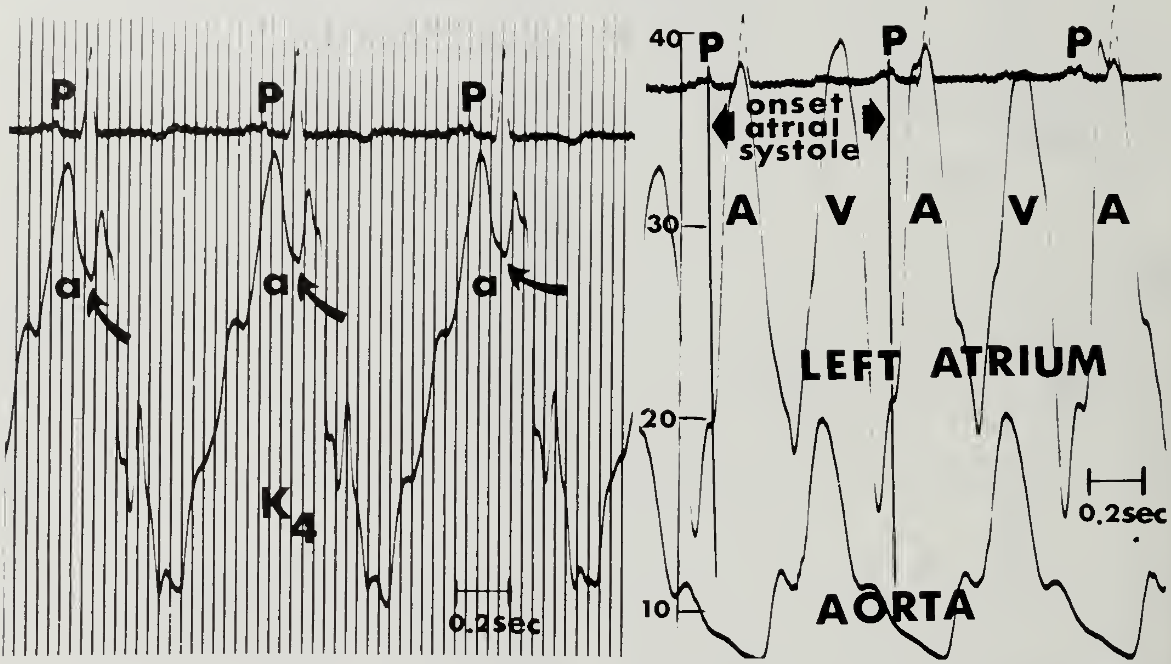

**FIG. 8.** W. J., a 38-year-old man with aortic regurgitation and a vigorous presystolic thrust palpable across the precordium from sternum to apex (case 7). Kinetocardiogram recorded at apex is shown on left panel. Entire diastolic filling period is characterized by rapid outward movement, culminating in the presystolic thrust (designated as "a"). Note that descending limb of this deflection merges with onset of a brief, normal outward movement of ventricular contraction (curved arrow). Right panel presents left atrial pressure pulse recorded with central aortic pressure pulse. Pressure scale is atrial. Note striking A and V pressure peaks, approaching 40 mm./Hg. The ascending limb of the A deflection corresponds in time to the presystolic precordial thrust ("a" depicted in the left panel).

Cardiac catheterization revealed a striking A wave in the left atrial pressure pulse with peak atrial systolic pressure ranging from 35 to 40 mm. Hg. Severe aortic regurgitation without stenosis was demonstrated. A small gradient was demonstrated across the mitral valve in early diastole and again during atrial systole. No mitral regurgitation was visualized on the left ventricular cineangiocardiogram. Comparison of kinetocardiogram and left atrial pressure pulse revealed that the onset of the giant atrial A wave corresponded in time to the presystolic precordial thrust (figure 8).

## Discussion

Each of these patients had a readily palpable outward thrust of the chest wall which occurred just before ventricular contraction. Although the movement was usually diffuse, the amplitude was maximum at either the apex or lower left parasternal region. Three patients exhibited movement only in the lower left parasternal region. One patient exhibited a readily discernible double movement to palpation; these 2 impulses were found to coincide with atrial systole and with late ventricular systole (figure 4). The impulse which occurred during ventricular relaxation in late systole was interpreted to represent ascent of the atrioventricular septa and atrial filling.[5]

Timing of the presystolic thrust, as recorded by kinetocardiography, was fairly uniform from patient to patient; the movement started 0.08 ± 0.02 second after the onset of the electrocardiographic P wave, reaching a peak at 0.13 ± 0.02 second after P. The presystolic deflection extended into the initial phase of the QRS complex, so that the descending limb was often interrupted by the movement of ventricular contraction. Separation of right from left atrial movement could not be accomplished with certainty from inspection of the kinetocardiograms alone. Thus, figures 2 and 7 depict a similar atrial movement, maximum in both cases at the lower left sternal border even though one patient suffered cor pulmonale with right atrial hypertrophy (case 2), and the other patient had hypertension and coronary heart disease with left atrial hypertrophy (case 6). In most patients the clinical setting readily determines which atrium is involved.

Mounsey[1] recorded an exaggerated presystolic thrust of the precordium in aortic and pulmonic stenosis, mitral regurgitation, primary myocardial diseases, and other disorders associated with diminished ventricular compliance. He reported the cineangiocardiogram of one such patient to demonstrate forward thrust of the left ventricle during vigorous atrial systole. In another patient with pulmonic stenosis direct observation at surgery revealed forward movement of the right ventricle during the brisk contraction of a hypertrophied right atrium.

Other studies have identified the phenomenon of palpable presystolic precordial thrust, calling particular attention to the bifid impulse, which results from the combination of presystolic thrust with the exaggerated systolic impulse of ventricular hypertrophy.[3] Goldblatt et al[6] described this movement pattern in aortic stenosis, while more recently Nagle et al[2] have stressed that atrial chest wall movement is particularly characteristic of obstructive cardiomyopathy. The cases reported herein confirm that presystolic movement occurs with a variety of heart diseases, may be present as the sole palpable impulse, and may constitute a vigorous thrust easily felt and seen.

The timing of this movement clearly relates it to atrial systole; contraction of the atrium begins during the descending limb of the electrocardiographic P at the same time that the outward deflection of the chest wall is recorded on the kinetocardiogram.

Since the atria do not directly contact the anterior chest wall it is likely that atrial systole contributes to the precordial impulse pattern by causing movement of the ventricle(s). That atrial systole causes ventricular forward movement is indicated by Mounsey's observations, cited above, as well as our observation in case 7, of a 35 mm. Hg A wave in the left atrial pressure tracing whose ascending limb corresponded in time to the presystolic chest wall movement (figure 8). Simultaneous left atrial and left ventricular pressure recordings in this patient disclosed a marked presystolic pressure rise in the left ventricle during atrial systole with elevation of the Z point to 35 mm. Hg (figure 9). It seems likely that vigorous contraction of the posteriorly located left atrium imparted forward movement to the left ventricle in this case.

The hemodynamic importance of atrial systole has been thoroughly reviewed in recent years, much investigation having been stimulated by the development of electrical pacing and cardioversion. Atrial contraction with normal atrioventricular conduction adds a significant increment to stroke volume in most patients with heart disease[7, 8] and clearly influences the loudness of the first heart sound. Of special interest to clinicians has been the atrial gallop sound, one of the most common extra heart sounds encountered in medicine. As its name implies, the atrial gallop coincides with atrial mechanical systole and can derive from either right or left atrial contraction.

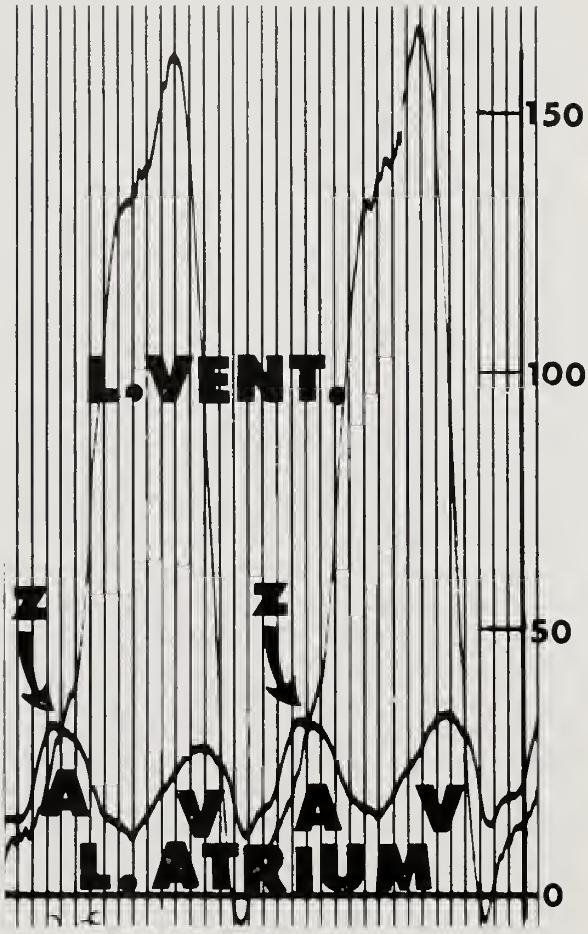

**FIG. 9.** Simultaneous left atrial and left ventricular pressure pulses in a 38-year-old man with aortic regurgitation (case 7). Atrial systole (A) causes precipitous rise in ventricular diastolic pressure from a mid-diastolic level of 5 mm. Hg to 35 at the onset of ventricular systole (Z). Forward movement of left ventricle, generated by thrust of contracting left atrium, is postulated to be the mechanism of presystolic chest wall movement. Note gradient between atrium and ventricle in early diastole and during atrial systole.

Rarely heard in health, this sound occurs either with atrioventricular block or with diseases characterized by reduced ventricular compliance.[6, 9]

A close relationship between the atrial gallop and the atrial thrust is suggested by their coincidence in time in several of the patients reported here (figures 1, 3, 5). The atrial sound commenced at the midpoint of the atrial impulse in these cases. A common genesis is also suggested by the conditions found in this study to be associated with presystolic movement—primary myocardial disease, hypertension, myocardial infarction, and cor pulmonale—conditions known to be associated with atrial gallop.

Patients 5 and 7 exhibited presystolic movement with mitral stenosis and aortic regurgitation respectively, conditions not usually associated with atrial gallop. Patient no. 7 has been discussed above (figures 9 and 10). Although patient no. 5 did not undergo cardiac catheterization, the clinical diagnosis of mitral stenosis seemed firmly established. The mechanism of presystolic precordial movement is not clear in this patient; it is likely that vigorous left atrial systole imparted forward motion to the left ventricle in spite of mitral obstruction. The physical signs did not justify incrimination of the right atrium in this process. Observations on other patients with mitral stenosis or mitral regurgitation have suggested that atrial pulsation is prominent when the left atrium exhibits little or no dilatation. It is of interest that patients with ruptured chordae tendineae, whose atria do not promptly dilate, exhibit atrial gallop rhythm, whereas patients with chronic mitral regurgitation and dilated left atria rarely have atrial sounds.[10]

A palpable atrial thrust probably carries significance similar to that of the atrial gallop, suggesting that vigorous atrial systole is acting upon a ventricle which is resistant to filling. Recordings obtained by Dimond and Benchimol[11] have demonstrated transient atrial thrust during angina pectoris and have correlated this movement with transiently elevated left ventricular end diastolic pressures. Resistance to ventricular filling might result, therefore, from increased diastolic pressure with or without increased stiffness of the ventricular wall.[6, 9, 11]

Additional clinical importance of this movement relates to its proper identification. Although simultaneous palpation and auscultation permit correct timing of precordial pulsations, few physicians practice palpation in this manner. Most of the impulses reported herein were misinterpreted clinically as ventricular systolic movements until the recordings were examined. Both right and left ventricular enlargement were simulated, as was the systolic bulge of myocardial infarction.

Once attention was drawn to the existence of this phenomenon, it proved possible to identify presystolic movement on palpation prior to recording. It is likely that many atrial thrusts are mislabeled. For example, a ventricular gallop which is thought to be palpable may in some instances represent mistimed atrial movement. More widespread correlation of precordial impulse records and clinical palpation may lead to further observations on this and related movement patterns.

## Summary

A prominent outward thrust of the chest wall has been identified to be related to atrial systole. This movement has been palpated over the lower left parasternal region, over the cardiac apex, and in some instances across the entire precordium. Although usually a single impulse, the movement may be followed by a ventricular systolic thrust, imparting a bifid sensation to the hand. The impulse results from a forward thrust of the ventricle(s) caused by exaggerated vigor of atrial contraction.

Atrial pulsation is demonstrable in a variety of cardiac disorders but is especially prevalent in diseases characterized by resistance to ventricular filling. Such resistance in the left heart may result from the reduced myocardial compliance of hypertension, aortic stenosis, or primary myocardial disease, or may result from the increased ventricular diastolic pressure of heart failure. Conditions causing resistance to right ventricular outflow, such as pulmonic stenosis or pulmonary hypertension, may also lead to palpable atrial thrust.

Atrial pulsation is often found in conjunction with atrial gallop rhythm; a similar genesis probably underlies these 2 physical findings. The movement is common but is often either overlooked or misinterpreted to be a ventricular systolic impulse. Simultaneous auscultation and palpation facilitate the proper timing of chest wall movements as does the graphic registration of precordial pulsation by means of an appropriate recording technique.

The authors wish to express appreciation to Dr. Robert F. Johnston of the Henry R. Landis State Hospital, Philadelphia, for his valuable coöperation and to Dr. Gerardo Voci of Woman's Medical College of Pennsylvania, who performed the cardiac catheterizations on patients nos. 2 and 7.

(*Continued on page 578*)

# Bacteremic Shock

WILLIAM J. MARTIN, M.D., F.A.C.P.*

Bacteremic shock refers to peripheral vascular collapse, the essential clinical manifestation of which is arterial hypotension, complicating bacterial invasion of the bloodstream. Bacteremic shock is said to be present when the following criteria are fulfilled: (1) A sustained, often precipitous, decrease in systolic blood pressure to 80 mm. of mercury or below is noted in an individual previously normotensive; (2) bacteria are recovered from blood cultures obtained during or shortly preceding the hypotension; and (3) the clinical picture is compatible with bacteremia while other causes of shock are excluded. The blood pressure may not faithfully reflect the status of the microcirculation to various body organs and, consequently, inadequate tissue perfusion may be present prior to the clinical detection of hypotension. Notwithstanding, sustained systemic arterial hypotension remains the essential clinical manifestation of bacteremic shock since more sensitive clinical methods of detection currently are unavailable.

Although shock of this variety often is emphasized as complicating bacteremia due to gram-negative bacilli, it may complicate other infections. Shock occurs in nonbacterial infections: viral (hemorrhagic fever), rickettsial (Rocky Mountain spotted fever), and parasitic (malaria). Shock also is encountered in nonbacteremic bacterial infections, such as cholera and shigellosis. Further, it complicates other bacteremias, such as staphylococcemia and meningococcemia.

## Physiologic and Pathologic Considerations

The pathogenesis of human bacteremic shock is incompletely understood. It is recognized that some types of shock occur in the absence of blood or fluid loss from the vascular system. Normal blood pressure reflects a satisfactory relationship of vascular capacity to blood volume, and significant change in either of these variables is reflected by a change in blood pressure. When vascular capacity is increased by dilatation of the vessels, blood is sequestered therein, and diminished amounts are returned to the heart. Incomplete cardiac filling may result in reduced cardiac output, hypotension, and diminished arterial blood flow. Consequently, there is inadequate perfusion of vital tissues and organs with oxygenated blood. Although definite proof is lacking, liberation of bacterial toxins into the systemic circulation probably initiates the complex pathophysiologic response present in bacteremic shock. Bacterial toxins apparently act indirectly on blood vessels through the medium of an unknown component in blood and induce tetany-like activity of the vascular beds near the arteriolar level. Initially vasoconstriction predominates, but alternating vasodilatation of progressive duration eventuates in vascular atony, stagnation of blood in the peripheral capillary beds, and consequent shock. The resulting decreased cardiac filling may eventuate in diminished arterial blood flow as previously noted, the consequence being that anoxia prevents normal cellular metabolism and that anaerobic cellular reactions dominate, with formation of acid metabolites, such as lactic acid and pyruvic acid, to the point of metabolic acidosis. The anoxic cells may release excessive amounts of potassium, resulting in hyperkalemia. Increasing amino-acidemia may manifest the anoxic liver's inability to metabolize the increased load resulting from tissue breakdown.

Shock after administration of bacterial toxins has been produced in experimental animals subsequent to decapitation, vagotomy, and chordotomy, apparently excluding the central nervous system from responsibility for the response. The intense spasm of hepatic veins with pooling of blood in canine livers apparently is not duplicated in man. Neither in experiments nor in humans is there evidence of adrenal failure, even when the subject is moribund.

It should be stressed that in bacteremic shock blood volume usually is adequate but perfusion is ineffective because of peripheral pooling. As data accumulate it becomes apparent that human bacteremic shock is not the result of a single hemodynamic aberration; some patients have reduced cardiac output and normal or increased peripheral arterial resistance, whereas others have high or essentially normal cardiac output and reduced peripheral arterial resistance.

Autopsy studies frequently do not reveal find-

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ings which might be considered specific or highly diagnostic of bacteremic shock. Lesions of the kidneys associated with renal insufficiency may include renal tubular necrosis, but in some cases nephrotoxins, such as certain antibiotics, might also be responsible. In a few patients there is a distinct lack of correlation between severe renal failure and morphologic alterations of the kidneys. In our observations we have not detected evidence suggestive of the generalized Shwartzman phenomenon, nor have we found unequivocal evidence of disseminated intravascular coagulation. Colonization of walls of small blood vessels by numerous gram-negative bacilli appears to be a specific finding in certain patients dying with Pseudomonas bacteremia. Hemorrhages into the adrenal gland may occur, and classically this finding is associated with meningococcemia, but hemorrhage also occurs in other forms of bacteremia.

## Bacterial Etiology

Although almost any bacterial species can produce bacteremia under certain circumstances, some species are more frequently responsible (table 1). Infections in which antibacterial therapy is unavailing are not considered herein.

History of any prior therapy (operation, glucocorticoids), knowledge of the existence of any underlying or predisposing disease (diabetes mellitus, cirrhosis), detection of a primary nidus of infection (pyelonephritis, cholangitis), and demonstration of certain physical findings (cellulitis, nuchal rigidity) may indicate the type of pathogen likely to be responsible for a given case of bacteremia.

For purposes of convenience, antibacterial regimens pertinent to the causative bacteria will be discussed in this section. A general summary of these drugs is shown in table 2. The drugs are listed in order of choice to parallel the severity of the infection whenever possible, and, for the most part, those in decreasing order are somewhat less effective or are more likely to be toxic. Of course, in some cases several agents are recognized as being effective. In certain instances a drug is preferred because one's experience with it is greater. Other drugs not listed may show some activity against a given bacterial species. Also, the antibacterial regimen selected for use in a given instance may reflect such factors as the patient's general condition and resistance, his allergic diathesis, and his ability to accept the regimen by the route designated. In general, combinations of antibiotics should be reserved for situations that demand treatment while microbiologic data are awaited, for polymicrobic infections, and for instances of bacteremia wherein there are indications that an enhanced effect is possible.

The principles of antibacterial management of patients having bacteremia can be summarized as follows: (1) procurement of samples of blood for adequate microbiologic study and initiation of treatment empirically if the condition of the patient warrants; (2) reëvaluation if in vitro bacterial susceptibility tests later indicate poor choice of an antimicrobial regimen, but continuation of the regimen unaltered if the patient is doing well; (3) in severe infections, procurement of serum bactericidal tests in a further attempt to determine if the bacteria are eradicable by the antimicrobial regimen employed, and (4) administration of the drug or drugs in adequate dosage for a sufficient time.

*Staphylococcal bacteremia.*[1] The best treatment remains penicillin G therapy, provided the organisms are susceptible to it. The need for agents with the potential of the penicillinase-resistant penicillins, such as methicillin, oxacillin, cloxacillin, and nafcillin, is not so great in staphylococcal bacteremia as in staphylococcal endocarditis. This is so because bacteriostatic agents, such as erythromycin and novobiocin, have been effective in staphylococcal bacteremia.[2, 3, 4]

In the following scheme an attempt is made to include all pertinent antistaphylococcal drugs and to indicate their possible clinical application. It is obvious that some of these drugs are less frequently employed at present, largely because the unavailability of microbiologic data (especially the results of in vitro susceptibility tests) often results in the use of a given drug and its continued use thereafter when the patient responds well. If such data were more speedily reportable, perhaps some of the potentially effective drugs in a given situation would be employed and one would be less concerned about emergence of bacterial strains resistant to the drugs more commonly used at present. There is, of course, no gross objection to the use of methicillin or an allied drug when cultures indicate a Staphylococcus organism to be the cause of bacteremia and before the results of susceptibility tests have been reported; when these results become available one can reëvaluate the regimen accordingly.

If the Staphylococcus resists the action of penicillin G (that is, if it requires more than 1.0 $\mu$g./ml. for inhibition) but is sensitive to erythromycin, this drug may be the agent of choice since it is virtually nontoxic. Next, one may wish to

**TABLE 1: Antibiotics of Choice in Bacteremia Due to Indicated Organisms**

| Organism | Antimicrobial Agents | | |
|---|---|---|---|
| | First Choice | Second Choice | Third Choice |
| *Staphylococcus aureus* | Bactericidal effect: penicillin G or a penicillinase-resistant penicillin | Vancomycin or cephalothin | Kanamycin, ristocetin, bacitracin, or neomycin and bacteriostatic agents |
| | Bacteriostatic effect: erythromycin or lincomycin | Novobiocin | Chloramphenicol |
| *Streptococcus pyogenes* | Penicillin G | Erythromycin | Cephalothin or lincomycin |
| *Streptococcus viridans* (*S. mitis, S. salivarius*) | Penicillin G alone or with streptomycin | Erythromycin | Cephalothin, lincomycin, novobiocin, or vancomycin |
| Enterococcus (*Streptococcus faecalis*) | Penicillin G or ampicillin with streptomycin or kanamycin | Ristocetin | Vancomycin, erythromycin-streptomycin |
| *Diplococcus pneumoniae* | Penicillin G | Erythromycin | Cephalothin, lincomycin or a tetracycline |
| *Neisseria meningitidis* (intracellularis) | Penicillin G | Erythromycin | A tetracycline or chloramphenicol |
| *Neisseria gonorrhoeae* | Penicillin G | A tetracycline | Erythromycin |
| *Escherichia coli* | Empiric therapy: a tetracycline and streptomycin | Empiric therapy: chloramphenicol-kanamycin | Polymyxin B or colistin |
| | Definitive therapy: ampicillin | Definitive therapy: cephalothin | |
| *Klebsiella-Aerobacter* | Empiric therapy: a tetracycline and streptomycin | Empiric therapy: chloramphenicol-kanamycin | Polymyxin B or colistin |
| | Definitive therapy: polymyxin B or colistin | Definitive therapy: cephalothin | |
| *Proteus mirabilis* | Empiric therapy: a tetracycline and streptomycin | Empiric therapy: chloramphenicol-kanamycin | Cephalothin or novobiocin |
| | Definitive therapy: penicillin G | Definitive therapy: ampicillin | |
| *Proteus vulgaris, morganii* and *rettgeri* | Empiric therapy: a tetracycline and streptomycin | Empiric therapy: chloramphenicol-kanamycin | Cephalothin |
| | Definitive therapy: kanamycin | Definitive therapy: chloramphenicol or cephalothin | |
| *Paracolobactrum* | A tetracycline and streptomycin | Kanamycin-chloramphenicol | Polymyxin B or colistin-cephalothin |
| *Alcaligenes* | A tetracycline and streptomycin | Kanamycin-chloramphenicol | Polymyxin B or colistin-cephalothin |
| *Salmonella typhosa* | Chloramphenicol | Ampicillin | A tetracycline |
| Other *salmonellae* | Ampicillin | Kanamycin | A tetracycline, chloramphenicol, polymyxin B, or colistin |
| *Shigella* | Ampicillin | A tetracycline | Kanamycin, polymyxin B, colistin, or chloramphenicol |
| *Pseudomonas* | Polymyxin B | Colistin | A tetracycline-streptomycin |
| *Bacteroides* (*B. fragilis, B. funduliformis*) | A tetracycline | Penicillin G | Chloramphenicol |
| Fusospirochetes (Vincent's) | Penicillin G | Erythromycin | A tetracycline |
| *Streptobacillus moniliformis* | Penicillin G | Erythromycin | A tetracycline |
| *Pasteurella tularensis* | Streptomycin | A tetracycline | Chloramphenicol |
| *Pasteurella pestis* | A tetracycline and streptomycin | | |
| *Pasteurella multocida* (*P. septica*) | Penicillin G | A tetracycline | Erythromycin |
| *Hemophilus influenzae* | Ampicillin | Chloramphenicol | A tetracycline and streptomycin |
| *Achromobacter* | A tetracycline and streptomycin | Chloramphenicol-kanamycin | Polymyxin B or colistin-cephalothin |
| Mimeae (*Mima polymorpha, Herrellea vaginocola*) | A tetracycline and kanamycin, polymyxin B, or colistin | | |
| *Clostridia* | Penicillin G | Erythromycin | A tetracycline |
| *Listeria monocytogenes* | Penicillin G | A tetracycline | Erythromycin |

**TABLE 2: Dosage of Antibiotics in Bacteremia**

| Agent | Route of Administration | | |
|---|---|---|---|
| | Oral | Intramuscular | Intravenous |
| Penicillin G (benzyl penicillin), and penicillin V or phenethicillin | Penicillin V or phenethicillin, 200,000 units (125 mg.)–800,000 units 4–6 times daily* | Aqueous crystalline penicillin G, 4,000,000–12,000,000 units daily | Penicillin G, 6,000,000 units or more |
| Methicillin | | 4–6Gm./day in 4–6 divided doses | 4–24 Gm./day in 4–12 divided doses |
| Oxacillin | 2–6 Gm./day in 4–6 divided doses* | 4–6 Gm./day in 4–6 divided doses | 4–24 Gm./day in 4–12 divided doses |
| Cloxacillin | 1–6 Gm./day in 4–6 divided doses* | Commercially unavailable in U.S.A. | Commercially unavailable in U.S.A. |
| Nafcillin | 2–6 Gm./day in 4–6 divided doses* | 4–6 Gm./day in 4–6 divided doses | 4–24 Gm./day in 4–12 divided doses |
| Ampicillin | 2–6 Gm./day in 4–6 divided doses† | 4–6 Gm./day in 4–6 divided doses | 4–12 Gm./day in 4–12 divided doses |
| Streptomycin | Poorly absorbed | 2 Gm./day in 2 divided doses not to exceed 2 wks. or 1 Gm. daily in 2 doses not to exceed 4 wks. | |
| Neomycin | Poorly absorbed | 1 Gm. daily in 4 doses | |
| Kanamycin | Poorly absorbed | 1–1.5 Gm./day in 2–3 divided doses | 1 Gm./day in 2 divided doses |
| Tetracyclines | 2 Gm./day in 4 divided doses‡ | Not recommended† | 1–2 Gm./day in 2–4 divided doses |
| Chloramphenicol | 3 Gm./day in 6 divided doses | 3–4 Gm./day in 3–4 divided doses | 2–4 Gm./day in 2–4 divided doses |
| Erythromycin (base) | 2 Gm./day in 4 divided doses | Not recommended† | 2–4 Gm./day in 2–4 divided doses |
| Novobiocin | 2 Gm./day in 4 divided doses | 2 Gm./day in 2 divided doses | 2 Gm./day in 2–4 divided doses |
| Lincomycin | 2 Gm./day in 4 divided doses | 1,200–1,800 mg./day in 2–3 divided doses | 1,200–1,800 mg./day in 2–3 divided doses |
| Polymyxin B | Poorly absorbed | 150–200 mg./day in 3–4 divided doses | 150–200 mg./day in 1–2 divided doses |
| Colistin | Poorly absorbed | 100–150 mg./day in 2–3 divided doses | 100–150 mg./day in 1–2 divided doses |
| Bacitracin | Poorly absorbed | 60,000–100,000 units/day in 4 divided doses (never more than 100,000 units daily) | |
| Vancomycin | Poorly absorbed | | 2 Gm./day in 4 divided doses |
| Ristocetin | Poorly absorbed | | 2–4 Gm./day in 2 divided doses |
| Cephalothin | Poorly absorbed | 4–6 Gm./day in 4–6 divided doses | 2–12 Gm./day in 4–6 divided doses |

* Oral use is begun only after the infection is controlled with parenteral therapy.
† Intravenous therapy preferred as parenteral therapy in this type of infection.
‡ Dosage of 1 Gm./day of demethylchlortetracycline or methacycline may suffice.

consider lincomycin or novobiocin. In the highly improbable situation that erythromycin, lincomycin, or novobiocin cannot be used, then methicillin or an allied drug may be the drug of choice. When these drugs are not applicable, as in patients who have a known allergy to the penicillins, cephalothin may be tried. Thereafter kanamycin may precede consideration of vancomycin because, although both are ototoxic, kanamycin is given intramuscularly whereas vancomycin is given intravenously; however, vancomycin is an effective antistaphylococcal drug and some workers would choose it over either kanamycin or cephalothin. Chloramphenicol follows in choice because of its propensity to depress the bone marrow; however, it precedes consideration of ristocetin, which also has a hematotoxic effect but has the added disadvantage of requiring intravenous administration. Before or after consideration of chloramphenicol and ristocetin (the decision may depend on one's fear of ill effects on the marrow or on the laboratory facilities that are available) one can consider combined antibiotic therapy. If such therapy is chosen, one of the so-called bacteriostatic agents, such as erythromycin or novobiocin, is used, together with a bactericidal agent such as bacitracin or kanamycin. However, the need for such cumbersome therapy is less frequent with the present availability of several effective antistaphylococcal agents.

Indiscriminate use of methicillin and allied drugs must be avoided. Since the degree of resistance to an agent is correlated with the amount of the drug being used in a geographic region, and since resistance to these agents has been demonstrated both in vitro and in vivo, the incidence of resistant strains probably will increase.[4]

As a generalization, antibacterial therapy of bacteremia due to staphylococci, like that due to most other bacterial strains, should be continued until the patient has been afebrile for at least 72 hours and 3 successive blood cultures have been negative.

*Streptococcal bacteremia.* This condition has been studied by members of our group,[5] and a group A beta-hemolytic Streptococcus organism (*Streptococcus pyogenes*) was responsible in about 50 per cent of cases. Group D nonhemolytic streptococci or enterococci, such as *S. faecalis*, were causative in 30 per cent of cases, while alpha-hemolytic or viridans streptococci, such as *S. mitis* and *S. salivarius*, were responsible in the remainder. I have not encountered an instance of bacteremic shock caused by viridans streptococci.

In the treatment of bacteremia due to *S. pyogenes* some workers give 1 million units of benzyl penicillin intramuscularly or by intermittent intravenous injection every 4 to 6 hours; other workers give even larger amounts of the drug by continuous intravenous administration. In bacteremia due to *S. mitis* and kindred organisms we are currently investigating a regimen of 1 Gm. of streptomycin given intramuscularly, plus 20 million units of benzyl penicillin given intravenously, per day; some workers believe that streptomycin is not required in these infections. Because most strains of enterococci are more resistant to penicillin G than are other streptococci,[6] usually we institute the same regimen outlined for infection due to *S. mitis* and allied organisms and increase the amount of benzyl penicillin in increments of 10 million units until the serum bactericidal test reveals total killing in a dilution of 1 to 4 or greater. In enterococcal bacteremia some workers prefer kanamycin to streptomycin. There are preliminary indications that ampicillin may be as effective as streptomycin-penicillin G as an anti-enterococcal regimen. An amount of 6 Gm. or more of ampicillin should be given daily by a parenteral route, preferably intravenously; streptomycin or kanamycin may further enhance the effect of ampicillin.

In patients allergic to the penicillins, such antibiotics as cephalothin, erythromycin, lincomycin, or a tetracycline may be applicable in cases of bacteremia due to *S. mitis* or kindred organisms. These drugs, excepting the tetracyclines, are also considered in bacteremia due to *S. pyogenes*; about 40 per cent of strains of *S. pyogenes* resist the action of the tetracyclines. A considerable number of enterococci resist the action of the alternate drugs, and one may have to rely on such antibiotics as vancomycin or ristocetin.

*Pneumococcal bacteremia.*[7] In the absence of pneumonia, endocarditis, or meningitis, pneumococcal bacteremia is unusual. Penicillin G is the drug of choice; the route of administration and daily amount, which may be several million units, are dependent in part on the presence or absence of associated endocarditis or meningitis. In patients allergic to the penicillins a drug such as cephalothin, erythromycin, or lincomycin may be given. Because some strains of pneumococci are resistant to the tetracyclines, use of these drugs in pneumococcal infections without in vitro susceptibility tests indicating their applicability may be hazardous.

*Neisserian bacteremia.*[8] This type of bacteremia is most commonly due to *Neisseria meningitidis*, the management of which virtually is inseparable from that of meningococcal meningitis. Benzyl penicillin in amounts of 1 million units every 2 to 4 hours by intramuscular injection may be used, but even larger amounts have been given per day intravenously. Since a number of strains of meningococci are resistant to the sulfonamides, these drugs cannot be relied on for initial management. *N. gonorrhoeae* rarely succeeds in invading the bloodstream, but large doses of penicillin G are recommended if invasion occurs. Although theoretically *N. gonorrhoeae* should be capable of causing bacteremic shock, I have no empiric knowledge of this occurring.

*Enterobacillary bacteremia.*[9-27] This has increased in incidence 3-fold to 5-fold in recent years. For purposes of convenience, in addition to the Enterobacteriaceae certain other gram-negative bacilli, such as *Bacteroides*,[17] *Pseudomonas*,[12] and *Achromobacter*,[13] will be considered under this heading. Of the Enterobacteriaceae, *Escherichia coli*[10] is encountered about twice as often as Klebsiella-Aerobacter organisms[11]; the remaining cases are most commonly due to Proteus bacilli.[9, 13, 20, 24, 25, 26] Other members of the Enterobacteriaceae which are less commonly responsible include Paracolobactrum, Alcaligenes, Salmonella, and Shigella. Pseudomonas organisms cause bacteremia about half again as often as Proteus organisms, whereas strains of Bacteroides cause bacteremia about half as frequently as do Proteus bacilli. Organisms of the Achromobacter family infrequently cause bacteremia.

Our practice is to initiate antibiotic therapy empirically after clinical examination or on receipt of reports of blood cultures positive for gram-negative bacilli. If in vitro susceptibility tests later indicate that the choice of treatment is less than optimal, the program is reëvaluated. A tetracycline combined with streptomycin or, in the more recent past, the conjoint use of chloramphenicol and kanamycin has been the empiric regimen most commonly employed by members of our group under these circumstances. Currently we are investigating colistin or polymyxin B given together with cephalothin, and thus far the combination has been very satisfactory.

Kanamycin-chloramphenicol is preferred when a staphylococcal co-infection is possible and sometimes is substituted when there has been poor response after a 12- to 24-hour trial of streptomycin-tetracycline. Also, one may prefer polymyxin B or colistin when there is underlying hematologic disease[19] or substitute one of these drugs when response is inadequate; in such cases the use of a tetracycline or chloramphenicol usually is continued, or it may be replaced by cephalothin therapy. In addition to their effectiveness against Pseudomonas organisms, polymyxin B and colistin have proved efficacious in infections due to other bacilli, such as *E. coli* and *A. aerogenes.*[12, 20, 24, 25, 26]

In cases of bacteremia likely due to gram-negative bacilli, empiric administration of these regimens, after samples of blood have been obtained for cultures, is preferred to therapy with a single drug. This is so because identification of bacteria and results of susceptibility tests will not be available for 1 or more days, and the broader antibiotic coverage is desirable. Also, there is the possibility that such combined therapy will provide an enhanced antibacterial effect. There is no dispute regarding the generalization that best results are obtained when the infecting organisms are susceptible on in vitro tests to the antimicrobial drugs employed, but the difficulty lies in the unavailability of such data when the clinical status of the patient makes initiation of therapy necessary.

With the advent of newer drugs we have reevaluated our policy of employing combined antibiotic therapy. Kanamycin, if used alone empirically, has the therapeutic inadequacy of not being effective against a number of Pseudomonas and most Bacteroides organisms. Colistin, like polymyxin B, has the objection, as a single agent, that Proteus and Bacteroides organisms usually are resistant. Ampicillin is inactive against most Proteus organisms that are indole-positive as well as against most Klebsiella-Aerobacter and Pseudomonas organisms. Cephalothin is not active against all Klebsiella-Aerobacter, Bacteroides, and indole-positive Proteus organisms and usually is inactive against Pseudomonas organisms. To date there is no single agent available that assures complete "coverage" against gram-negative bacilli.

Occasionally, although empiric therapy is sufficient to prevent death the response is incomplete; then microbiologic data may indicate possible use of a single agent. In other words, when the patient is not doing well clinically, the empiric regimen is replaced with the following drugs in keeping with the results of the in vitro susceptibility tests. Ampicillin, cephalothin, polymyxin B, or colistin may be applicable in infections due to *E. coli*; except for ampicillin, the same drugs are considered against Klebsiella-Aerobacter organisms. As a generalization, strains of *E. coli* are susceptible to streptomycin, the tetracyclines, and cephalothin in about 50 per cent of cases; these bacilli are susceptible to kanamycin, chloramphenicol, ampicillin, polymyxin B, and colistin in 80 per cent or more of cases. The same generalization is applicable to Klebsiella-Aerobacter organisms except that only about 10 per cent of these bacilli are susceptible to ampicillin. Penicillin G, ampicillin, cephalothin, and novobiocin are active against the indole-negative *P. mirabilis*, which causes 80 to 90 per cent of clinical infections due to Proteus organisms. While cephalothin and chloramphenicol may prove active against certain indole-positive Proteus organisms, that is, *P. vulgaris*, *P. morganii*, and *P.*

*rettgeri*, as a generalization kanamycin is the drug of choice against these bacilli.

In regard to salmonellosis, typhoid fever appears to remain well managed with chloramphenicol. However, while chloramphenicol is favored over ampicillin in the control of fever and early symptoms, there are some data indicating that the use of ampicillin may be followed by fewer relapses. In bacteremia due to other Salmonella organisms, a tetracycline, ampicillin, or kanamycin may be preferable, depending on in vitro susceptibility tests. Treatment of Salmonella bacteremia should be continued for 14 days.

Shigellosis, unlike salmonellosis, almost always is a purely intraluminal enteric infection. However, about 50 cases of Shigella bacteremia have been documented to date. In such patients tetracycline-streptomycin or chloramphenicol-kanamycin therapy has been suggested; ampicillin might be applicable.

In Pseudomonas bacteremia, polymyxin B or colistin is the drug of choice. In patients with such conditions as advanced malignant, hematologic, or renal disease, no form of current antimicrobial therapy is capable of preventing death in most cases. In patients not having such underlying conditions the mortality rate is 20 to 25 per cent.[24]

Organisms in the family of Bacteroides include *B. fragilis*, *B. funduliformis* (necrobacillus), fusospirochetes, and *Streptobacillus moniliformis*. Failure to obtain anaerobic cultures of the blood may conceal the fact that bacteremia due to members of the Bacteroides family may be present. In two-thirds of our patients with such bacteremia, incubation times ranged from 5 to 20 days.[17] It is our clinical experience that, as is true of Salmonella infection, bacteremia due to Bacteroides organisms requires more time for therapeutic control than do other gram-negative bacillary infections of the blood, and treatment should be given for 14 days. In the management of bacteremia due to either *B. fragilis* or *B. funduliformis* a tetracycline is effective; penicillin G may be active against some strains. In bacteremia due to *S. moniliformis* and in the rare instance of infection of the blood due to fusospirochetes penicillin G is recommended.

Achromobacter bacteremia has responded to streptomycin-tetracycline therapy. In certain cases in vitro susceptibility tests may indicate a more pertinent regimen.

*Pasteurella bacteremia.* This bacteremia is exemplified by those cases of tularemia in which *Pasteurella tularensis* invades the bloodstream. Tularemia is one of the few diseases in which streptomycin is employed alone with excellent results; the tetracyclines, chloramphenicol, and kanamycin also are effective antitularemic drugs. Streptomycin-tetracycline is the regimen of choice in plague. In bacteremia due to *P. multocida* (*P. septica*) penicillin G is recommended; in patients allergic to the penicillins erythromycin or a tetracycline is advised.[3]

*Influenzal bacteremia.* This is not infrequent in serious infections, such as meningitis due to *H. influenzae*. Ampicillin or chloramphenicol is preferred, especially in rapidly progressive infections.[2, 3, 4]

*Mimeae bacteremia.* This type of bacteremia, which may be due to either *Mima polymorpha* or *Herrellea vaginocola*, is treated with a tetracycline combined with kanamycin, polymyxin B, or colistin, at least until in vitro susceptibilities are reported. Reliance on a tetracycline alone, or tetracycline-sulfonamide therapy, no longer seems advisable.[2, 3]

*Clostridial bacteremia.*[28] This may occur in patients with underlying hematologic disease and in patients with neoplastic disease, but the majority of reported cases have been associated with postabortal or puerperal sepsis. Placing the patient in a hyperbaric chamber is essential. Penicillin G in massive doses is the antibacterial agent of choice, but some workers believe that a tetracycline should also be given. Surgical extirpation of a septic focus, blood transfusions, and polyvalent gas-gangrene antitoxin also may be considered.

*Listeria bacteremia.* Although this type of bacteremia may complicate neoplastic disease and diabetes mellitus, it has a propensity to occur during pregnancy. Infection due to *Listeria monocytogenes* may cause bacteremia in the infant while the mother is asymptomatic or has had an influenza-like illness. Penicillin G or a tetracycline is recommended.[2, 3]

*Polymicrobic bacteremia.* Such an infection is most likely to occur in infections of the blood due to *S. faecalis*,[5] Bacteroides[17] and Pseudomonas.[12, 24, 25, 26] Polymicrobic infections are of higher incidence in patients having Pseudomonas bacteremia because many of these victims have underlying hematologic disease. In the treatment of polymicrobic bacteremia several drugs may be given simultaneously, for example, penicillin G and streptomycin in enterococcal bacteremia and, concomitantly, a tetracycline or chloramphenicol against *E. coli* or Klebsiella-Aerobacter organisms. Also, in addition to a tetracycline in Bacteroides infection one may add penicillin G against streptococci. Perhaps ampicillin and cephalothin will have special application in future cases.[4]

### Symptoms and Signs of Bacteremic Shock

The clinical manifestations are synopsized by the crisscross of climbing temperature and pulse rate and declining blood pressure and urinary output.[23] There are 2 symptomatic and prognostic stages. In stage I, wherein the prognosis is better, the subject is alert but often restless and has warm, flushed skin, with full and bounding pulse, progressive pyrexia, and moderate hypotension; but urinary output is maintained. In stage II, wherein the prognosis is graver, the subject is pallid and has cold, damp extremities, collapsed superficial veins, feeble pulse, perhaps declining temperature, shallow hyperpnea, severe hypotension, and oliguria. Frequently there is a reduction in urine flow to 20 ml. or less in 1 hour. Ominous manifestations are cyanosis of the acral parts, cutis marmorata, perhaps purpura, Cheyne-Stokes respiration, gallop rhythm, hypothermia, refractory hypotension, dilated and sluggish pupils, hyporeflexia, coma, jaundice, progressive azotemia, and anuria.

In stage I signs of infection dominate those ordinarily indicating shock; at this stage hypotension may be the sole physical manifestation of a potentially lethal situation. If the process is identified in stage I and treated promptly, these paradoxical signs may not be replaced by those more characteristic of shock. Supervention of pallor, collapse of veins, hyperpnea, weakness of pulse, and curtailment of urinary output indicate increasing peripheral stagnation, with decreasing venous return and cardiac output.

Ecthyma gangrenosum (maculo-vesiculopustular lesions in the anogenital region and axillae),[12] petechiae, and a high incidence of jaundice may characterize pseudomonal infection. Diarrhea is suggestive of infection due to gram-negative bacilli, and especially Bacteroides or Salmonella organisms. Foul-smelling exudates, delayed response, and metastatic suppuration also may characterize Bacteroides bacteremia.[17] When bacteremia complicates septic abortion, one considers coccal and clostridial infection, but gram-negative bacilli commonly are responsible; smears of the cervix may aid in this distinction prior to the reports of blood cultures.

Leukocytosis is usually present, but a normal number of leukocytes is not rare. In an occasional case leukopenia shortly replaced by leukocytosis is the initial manifestation of complicating shock. In some cases of established Pseudomonas bacteremia, marked and persistent leukopenia occurs.[12, 24, 25, 26]

Azotemia, hyperkalemia, and decreased values for serum sodium, chloride, and carbon dioxide-combining power are common findings. Recently, the concentrations of lactate and pyruvate in the blood have been studied as possible indices of impending shock and its reversibility.

Metabolic acidosis, which is common in bacteremic shock, may be due largely to an increase in concentration of lactate radicals. As a preliminary impression the severity of shock appears to parallel the concentration of blood lactate; a high level of blood lactate or lacticacidosis, as it has been called, early in shock appears to indicate a poor prognosis.[29] An initial value of less than 10 mEq./liter, which drops rapidly with treatment, may indicate a better prognosis. Significant lacticacidosis occurs when the ratio of lactate to pyruvate is greater than 10 to 1. The correlation appears to be good between rising levels of blood lactate and decreasing values for serum bicarbonate and arterial pH. The genesis of lacticacidosis appears to reflect tissue hypoxia, resulting from reduced blood flow, which increases anaerobic metabolism and leads to a consequent rise in lactate levels. An elevated value for serum phosphate in the presence of acidosis may indicate lacticacidosis. A corroborative test of significant lacticacidosis is the determination of the anion gap ($Na + K - HCO_3 + Cl = 17$ mEq./L) wherein a gap greater than 17 is taken as being representative of true acidosis. Removal of lactic acid from the blood appears to be a function of the liver, and consequently lacticacidemia may occur when the blood supply of the liver is impaired or the liver is damaged by disease. In such patients as those having impaired renal function or diabetes mellitus, one should not fail to consider the multiple factors in the genesis of the acidosis.

### Diagnosis

In chronic infection of the urinary tract complicated by bacteremic shock it is often difficult at first to determine whether azotemia chiefly reflects the complication or the terminal renal insufficiency due to the primary nephropathy. It may be that the prognosis is graver in patients having chronic infection of the urinary tract, because either the hypotension precipitates terminal renal insufficiency resulting from the primary disease or the previously damaged kidneys fail to recuperate with sufficient rapidity. Compromising the kidneys by the twin factors of chronic infection and acute ischemia may explain the observation that bacteremic shock is of graver prognosis if associated with a urinary portal for the infection. In infections with a urinary portal, renal function, necessary for recovery, is more likely to remain intact or to be restored sufficiently in the period of grace by supportive therapy, so that antibacterial therapy is given the opportunity of eradicating the bacteremia. The function of kidneys previously damaged by infection may not be restored in the same period of therapeutic grace.[14, 21]

Likewise, severe hepatic disease seems to hinder recovery. And, as increasing azotemia may manifest the further insult to previously damaged kidneys, the addition of vascular collapse to hepatic disease may result in increasing aminoacidemia and jaundice. Occasionally, recognition of bacteremia and speedy initiation of pertinent therapy may have a lazarean effect in patients having so-called hepatic coma.

A shocklike state in a diabetic can be confusing; in addition to bacteremia, possible causes include so-called diabetic acidosis, cerebrovascular accident, and meningitis. Physical examination with emphasis on use of the thermometer and sphygmomanometer may provide the diagnosis before report of laboratory procedures.[16, 18]

## Treatment

Management of bacteremic shock[14, 21, 24, 25, 26] presumes close scrutiny of potential candidates, since prompt detection and treatment considerably decrease the mortality rate. Increases of temperature and pulse rate associated with decreases of blood pressure and urinary output in such patients dictate the need for empiric therapy after obtainment of samples of blood for culture if no other explanation is immediately forthcoming. In addition to antibiotic therapy, which is essential for eradication of the infectious cause of the shock in these cases, there are numerous ancillary measures which have been employed.

Although considerable controversy exists regarding ancillary procedures employed in various antishock regimens, those measures that are frequently recommended will be mentioned. Although any outline of such therapy is controversial, different regimens are being employed in several medical centers, and comparative data should become available. At the outset it should be recalled that differences in animal species, especially those between the canine and human, in their reactions to bacterial toxins make it extremely difficult to precisely relate experimental data to clinical phenomena. Use of various agents to improve blood flow and tissue perfusion in bacteremic shock cannot be directed by generalization but depends upon precise identification of hemodynamic derangements present in the individual patient.

Important among supportive measures is the management of fluid and electrolyte deficits. Although glucose given parenterally appears to prolong life in experimental animals, overadministration of fluids, especially of saline, during oliguria can embarrass cardiac function and induce pulmonary edema. Of course, if hypovolemia is present it should be corrected. Measurement of central venous pressure indicates the competence of the heart to accept and expel a given blood volume and may serve as a guide to volume repletion. Fluid can be cautiously given as long as the central venous pressure is low or normal, that is, 5 to 15 cm. of water.

Replacement of blood may be required in such patients as those with bleeding lesions of the gastrointestinal tract or with underlying hematologic disease. In these patients it is conceivable that reduced blood volume predisposes them to the development of shock from bacteremia, as is suggested in certain animal experiments.

Anti-acidotic measures are being investigated, and whereas acidosis can be corrected by infusion of sodium bicarbonate, levels of blood lactate appear to be uninfluenced unless the peripheral circulation is improved concurrently. In patients with lacticacidosis, other buffering agents, such as tris (hydroxymethyl) aminomethane or THAM, are being investigated. An isotonic solution of THAM (36 Gm. in 1,000 ml.) is given intravenously during 1- to 2-hour periods. A possible means of lowering blood levels of lactic acid is the administration of 5 per cent carbon dioxide in oxygen. Also there are experimental data that one may reduce lacticacidemia by the administration of dihydroxyacetone, a product of glucose metabolism that transforms lactic acid into pyruvic acid.

The gallbladder, postoperative wounds, obstructive uropathy, and so forth may constitute nidi of infection from which the blood is reseeded with organisms, and surgery may be required. One attempts to control the bacteremia before subjecting the patient to added stress, but sometimes bacteremia persists until such a nidus is attacked surgically. Metastatic suppuration requiring surgical attention most often complicates bacteremia due to *Staphylococcus aureus*, *Streptococcus pyogenes*, and Bacteroides organisms.[8]

Vasopressors have been used in an attempt to restore circulating homeostasis by reinforcing the natural body reaction, to prevent so-called irreversible shock, and also to forestall renal ischemia and renal shutdown. Use of a vasopressor is a temporary supportive measure until other therapeutic procedures and the patient's own compensatory mechanisms are able to maintain adequate blood pressure and tissue perfusion. Of the numerous vasopressor agents available, those which have been used commonly in the recent past include metaraminol (Aramine®), levarterenol or norepinephrine (Levophed®), and angiotensin (Hypertensin®). Of course, a current question is whether vasodilators should be used rather than vasopressors.[30-33]

Prior to further discussion of vasoactive drugs it may be well to review some of the terminology currently employed in describing these agents and their actions. There are 2 types of adrenergic receptors situated in blood vessels, alpha and beta. Alpha-adrenergic receptors mediate vasoconstrictor responses, whereas beta receptors mediate vasodilatation. Thus, levarterenol may cause vasoconstriction by stimulating alpha receptors in blood vessels whereas isoproterenol (Isuprel®) may cause vasodilatation by stimulating beta receptors. In addition, both levarterenol and isoproterenol may cause positive chronotropic effects (increased cardiac rate) and positive inotropic effects (increased myocardial contractility) via their action on the heart. Alpha-adrenergic blockers (alpha-receptor blockers), which may antagonize vasoconstrictor effects, are exemplified by phenoxybenzamine (Dibenzyline®) and phentolamine (Regitine®).

Metaraminol can be given intramuscularly, but preferably intravenously, in amounts of 100 to 250 mg. in 500 to 1,000 ml. of fluid. Experimental data indicate that the release of levarterenol from sympathetic nerves has a major part in the action of metaraminol. Reserpine may deplete body stores of levarterenol, with consequent reduced response to metaraminol.

Levarterenol is given intravenously in increments of 4 ml. of a 0.2 per cent solution in 1,000 ml. of 5 per cent dextrose in distilled water at a rate sufficient to maintin the desired blood pressure. The site of infusion and the course of the vein infused are observed for blanching; necrosis is minimized on stopping the infusion and infiltrating the area with adrenergic blocking agents such as phentolamine or piperoxan. In contradistinction to the reaction in normal subjects, in patients who are in shock administration of levarterenol and metaraminol tends to increase cardiac output.

Angiotensin has been given intramuscularly, but usually it is given intravenously. A vial of angiotensin contains 2.5 mg. of the drug, and 1 to 4 vials are added to 500 to 1,000 ml. of fluid. Angiotensin directly increases peripheral resistance without affecting the heart, and its action appears to be independent of adrenergic receptors. Patients not responding to levarterenol have responded to angiotensin, but the converse also occurs.

A Y-tube apparatus used in the intravenous administration of a vasopressor allows its periodic discontinuation so that only the minimum is consumed, and yet the drug is immediately available if hypotension occurs. Similar titration is not possible when vasopressors are given intramuscularly. When vasopressors are given it is unnecessary to raise the systolic blood pressure above 100 mm. Hg in a previously normotensive patient.

As aforementioned, vasodilators, including alpha-adrenergic blocking agents,[30-33] are being investigated as substitutes for vasopressors in patients having bacteremic shock. Proponents of their use point out that pallor, sweating, and tachycardia reflect vasoconstriction, and these workers discourage administration of vasopressor drugs because of concern that a further reduction in systemic blood flow might result. They postulate that dilatation of blood vessels rather than their further constriction by vasopressors is required to relieve visceral pooling. Phenoxybenzamine administered intravenously in amounts of 1 mg./Kg. of body weight is commonly recommended by these investigators; it has only recently become commercially available in this form. Although use of phenoxybenzamine may increase the urinary output it may also further reduce the blood pressure and require administration of blood or its products or a plasma expander to combat the increased hypotension. For this reason it is recommended that vasodilators be used only when effective circulating blood volume is known to be normal or is being replaced.[31] Despite considerable discussion based on animal experimentation there is a paucity of data on the efficacy of alpha-adrenergic blocking agents in the management of human victims of bacteremic shock. Eckenhoff and Cooperman[32] gave phenoxybenzamine to 24 patients, 6 of whom died; excessive vasodilatation was considered a contributory factor in the deaths of 5 of these 6 patients. Phentolamine is also an alpha-adrenergic blocking agent which has been employed for its vasodilating effect.

Isoproterenol is chemically related to epinephrine and levarterenol but, as aforementioned, is a so-called beta-receptor stimulator which may induce peripheral vasodilatation. The drug is used in cardiogenic shock and is currently being reëvaluated in bacteremic shock.[33] Monitoring of cardiac rhythm is advised during administration of the drug since arrhythmias may result from its inotropic effect. Isoproterenol is given intravenously in an initial dose of 2.5 mg. in 500 ml. of 5 per cent dextrose in water at a rate of 0.5 to 1 ml. per minute. If no reaction occurs within 15 minutes the rate of infusion is doubled.

Other vasodilators that have been recommended include trimethaphan (Arfonad®) and hydralazine (Apresoline®).[31]

There is some reticence to the abandoning of vasopressor use because evidence exists that the mortality rate is less for patients having bacteremic shock who receive vasoconstrictor drugs. Hall and Gold[34] reported a mortality rate of 57 per cent for 21 patients who did not receive vasopressor drugs and 36 per cent for 14 patients who were given these agents. Hodgin and Sanford[35] in their more recent study also concluded that use of vasopressor agents was of value in bacteremic shock. A possible basis for the discrepancy in opinions regarding the use of vasopressors is that less than desirable results have been noted in patients who have reached stage II of shock.

Oxygen therapy is an attempt to counteract tissue anoxia due to reduced arterial blood flow, and although it is helpful in experimental animals the logic of its clinical use is disputed. Hyperbaric oxygenation also has prolonged life in experimental animals, and theoretically it may increase oxygen transport to the tissues and have a bacteriostatic effect on the infecting bacilli. A major objection to the clinical use of hyperbaric oxygenation is the possibility of fatal oxygen toxicity involving the pulmonary and central nervous systems. An airway is provided if necessary.

Digitalization of the hypotensive patient is carried out only if the central venous pressure remains above 15 cm. of water and particularly if other evidences of heart failure, such as pulmonary edema, are detected.

Such mechanical measures as elevating the foot of the patient's bed and applying an abdominal binder and leg bandages may increase venous return and cardiac output. However, there are no exact data indicating that these measures are of substantial benefit.

The exact application of hypothermia[36,37] in bacteremic shock remains unclear, although it has been helpful in experimental animals. The rationale for hypothermia is based on reduction of the need for cellular oxygenation, thereby favorably influencing the metabolic environment. If hypothermia is not used the patient is kept comfortably warm, but overheating, which may dilate superficial vessels and further increase the capacity of the vascular bed, is avoided.

In some patients, especially when hypotension is prolonged, renal shutdown occurs. Usually recovery from renal shutdown is heralded by reappearance of excretory function within 10 to 12 days. However, excretory function reappears before regulatory function, and death with progressive azotemia and acidosis remains possible. Hemodialysis has contributed to maintaining life and reducing morbidity during the oliguric phase of renal shutdown.[38] It should not be reserved as a last desperate measure, since its failure to prevent death may reflect belated use. In this same regard there are data indicating that renal failure which is partial or incipient may be reversed by the intravenous use of mannitol. Significant diuresis is an average increment in urine flow of more than 0.2 ml. per minute in 3 hours after 25 Gm. of mannitol is given intravenously. If less than 50 ml. of urine is produced in the next 2 hours, no more mannitol should be given. The mechanism of mannitol diuresis appears to be acute expansion of blood volume, with subsequent increase in glomerular filtration rate. Lack of significant diuresis after administration of mannitol usually indicates fully developed renal shutdown. Concentrates of mannitol should not be given in the presence of hyponatremia or hypochloremia; the use of these concentrates also is not advisable in the presence of congestive heart failure.

Use of morphine, meperidine (Demerol®), barbiturates, and other depressants is best avoided.

Use of adrenal glucocorticoids has been advocated despite the fact that patients in bacteremic shock, even when moribund, show no abnormality of the secretory function of the adrenal gland.[39,40] It was generally assumed that the glucocorticoids would have special application in the syndrome of shock associated with severe meningococcal infections, but unfortunately this has not proved to be the case. Some investigators oppose administration of vasopressors on the basis that the adrenal glands are capable of providing these in sufficient quantity, but, contrariwise, some of these workers give massive doses of adrenal glucocorticoids despite no evidence of adrenal insufficiency. On reviewing mortality rates in reported series of bacteremic shock due to gram-negative bacilli wherein steroids were used, one might conclude that patients receiving them have a higher mortality rate. Known complications of steroid therapy include impairment of the immune response and an increased susceptibility to upper gastrointestinal bleeding; the latter complication can lead to considerable diagnostic and therapeutic confusion. Such bleeding occurs spontaneously in victims of bacteremic shock and may be potentiated by steroids. An additional objection to the use of such therapy is that, on analysis of the causes of death in patients having bacteremic shock due to gram-negative bacilli and given adrenal glucocorticoids, a complicating staphylococcal superinfection is not uncommon. I have limited administration of adrenal glucocorticoids in nonpharmacologic dosage to those patients who were receiving them prior to the onset of bacteremia.

Also, I have not used blood or its products in the definitive management of this complication, because in the usual case of bacteremic shock there appears to be no decrease in blood volume but rather stagnation and faulty redistribution of it. But a rapid intravenous infusion of 500 ml. of low molecular-weight dextran[41] in patients with a normal central venous pressure but low cardiac output and hypotension appears to be relatively safe and may normalize the circulatory dynamics without the need for a vasopressor. Depending on individual circumstances the dextran has been given over periods ranging from 30 to 120 minutes; 500 ml. can be administered slowly over subsequent 12-hour periods. Low molecular-weight dextran (40,000) has only recently become commercially available in the United States. Normally, dextran-40 is excreted in 1 to 2 hours, but in shock its excretion may be prolonged to 4 hours or longer. Administration of the agent may increase cardiac output, decrease peripheral resistance, and restore urinary output.

Heparinization to counteract intravascular coagulation during experimental bacterial shock has been advocated, but its benefit also lacks clinical confirmation. Numerous other regimens, including testosterone, aldosterone, serotonin antagonists, chlorpromazine, and even antihistamines have been described as being helpful in experimental animals, but this does not automatically assure their efficacy in the human subject.

It may be well to point out that overemphasis of a unitarian concept of shock with insufficient attention to etiologic differences may lead to regimens largely based on wishful thinking. At this time there is no single regimen equally applicable to such diverse etiologic entities as cardiogenic, hemorrhagic, and bacteremic shock. Cardiac support and replacement of blood do not influence the basic defect in the usual case of bacteremic shock, and these and other symptomatic procedures are designed only to maintain the patient's life until antibiotic therapy can control the overwhelming infection which is the essential cause of his vascular collapse. It is appreciated, of course, that patients with such underlying conditions as coronary artery disease and bleeding lesions of the gastrointestinal tract may require special attention in this regard, but these isolated requirements do not appear to warrant universal administration of digitalis and blood.

## Prognosis

The prognosis is considerably determined by the nature and severity of the initial lesion, the presence of underlying or predisposing disease, prior therapy, the duration of the infection before institution of appropriate management, and the occurrence of additional complications such as renal shutdown, metastatic infection, and superinfection.

Patients who recover usually have had the benefit of early diagnosis and treatment, and consequently potential candidates must be recognized and managed accordingly to ensure the best prognosis. Along with monitoring of the candidate's temperature and pulse rate, hourly determinations of the blood pressure and recording of the urinary output appear to be the best routine objective indices of his current status.

Prognostic considerations and evaluation of therapeutic regimens should include analysis of associated conditions, since frequently death from bacteremic shock appears to have been but a terminal event in a potentially lethal situation.[27] In this regard, one should be prepared to encounter the potential paradox that as man's ability to prolong life improves, his success in the management of bacteremic shock, especially that due to gram-negative bacilli, may decrease. This is so because the underlying disease predisposing to infection may so diminish host resistance that recovery is virtually impossible, at least within the present limits of therapy.

## Summary and Conclusions

Bacteremic shock may present signs such as warm, flushed skin, full-bounding pulse, fever, and alertness that ordinarily are not associated with shock due to other causes; only hypotension may corroborate supervention by this potentially fatal complication.

Antibiotic therapy is begun empirically when report of blood cultures is received or, in seriously ill patients, after blood is drawn for cultures. If the patient's condition and microbiologic data later indicate that such empiric therapy is unsatisfactory, it is modified accordingly. Use of specific antibiotics in the initial management of these patients is only theoretically possible because, practically, one is often thwarted by lack of cultural proof of the pathogen and, almost always, of its in vitro susceptibilities. However, these difficulties are not of such magnitude that one cannot devise adequate antibiotic therapy on an empiric basis. If such a regimen is not employed, or not employed early in the infection, the essential problem is not being attacked, and recovery is unlikely.

To the present, the majority of our patients with bacteremic shock have received a vasopressor and antibiotic therapy; they have not received adrenal glucocorticoids as definitive therapy. Members of our group plan to continue management of bacteremic shock in this manner, at least until sufficient data are available which would make a change in therapy reasonable. At the same time, in selected patients we are continuing our evaluation of various procedures, including isoproterenol (Isuprel) as an antihypotensive agent and the rapid infusion of dextran in place of a vasopressor. Perhaps more important than the investigation of new regimens is the recognition of the potential candidate and the monitoring of his temperature, blood pressure, and urinary output so that early diagnosis and treatment of the complication are possible. It is our experience too that when stage II of shock has been reached, optimal response to therapy is less likely. Such factors as blood loss and impaired cardiac function undoubtedly have a part in individual cases of bacteremic shock, and in such cases therapy should encompass these considerations, but this does not appear to be a reasonable basis for recommending that these therapeutic facets be generally applied.

It should be emphasized that one must guard against losing valuable therapeutic time while procuring multiple electrocardiograms, awaiting the results of laboratory procedures, and belatedly diagnosing bacteremic shock when the patient has not responded to regimens more pertinent to noninfectious shock. If bacteremic shock is not diagnosed early and if adequate antibiotic therapy is not quickly initiated, no supportive treatment will have optimal effect.

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*(Continued on page 578)*

# The Internist—Some Philosophical Comments

JOSEPH E. BRACKLEY, M.D., F.A.C.P.*

THE INTERNIST is a physician who is trained in the diagnosis and management of medical cases with due regard to the environment and personality of the patient. Some of the problems which the patient has may be on the bases of religion, racial or national custom, disparity of education within the family, or a person's displeasure with his environment. In order to treat these basic difficulties one must cultivate some knowledge of sources from whence they spring. Therefore, one must have some knowledge of historical, racial, theological, philosophical, and educational systems, with a great respect for the impacts of these systems on the individual. In the United States the Catholic physician must have some knowledge of the theology of Niebuhr and Tillich, the non-Catholic physician some understanding of St. Thomas and Duns Scotus. Both must have a knowledge of the Jewish Talmud. It is presumed that the Japanese physician understands Shintoism, Confucianism and Buddhism, as all of these may have an effect on a given patient. In short, one must understand the differences in educational, religious and racial milieu.

In the case of a patient who has recurring symptoms of anxiety, despite frequent discussion and reassurance, the internist may have to resign himself to the fact that he may be dealing with a patient who will need constant support over the years. This constant support may have to be of the most intensive variety, continuously applied. On other occasions it may be episodic, perhaps not so intense, but it may have to be applied for months or years, or, in fact, for a lifetime. It may have to be carried on by another physician after the original physician has died. In common with other physicians, the internist may desire rapid diagnosis, rapid treatment, and rapid resolution of the problem, but in many of his cases he must resign himself to constant support of the patient for long periods of time.

Along with this constant association with the problem patient over the years is the necessity of keeping the patient fully informed as to his diagnosis. It is my belief that some of the most discouraging diagnoses, such as malignancy, certain types of heart disease, and the collagenous diseases, which pursue a chronic course and may result in a lethal end, should be discussed with the patient and that a correct diagnosis be given in each case. I have never seen a patient deteriorate more rapidly because a correct but prognostically bad diagnosis was given, but I have seen situations greatly complicated when a diagnosis reasonably made was not told at the proper opportunity to the patient. This is sometimes an unpleasant duty, but once the patient is informed he or she usually accepts it quite well and has a period of time to prepare for death, dispose of his worldly affairs, and make plans for members of his family; furthermore, this patient does not distrust the informing physician. Needless to say, one must be accurate in making a diagnosis of poor prognosis because one does not want a patient to suffer for a period of time under the influence of an incorrect diagnosis. If a diagnosis is reasonably made, the patient should be informed.

Withholding a correct diagnosis, especially a potentially lethal diagnosis, from a patient is inherently bad because it insults the intelligence of the patient, who can scarcely understand rather complicated methods of treatment for a relatively innocuous disease. Furthermore, if concealment of a diagnosis is made and this diagnosis is revealed to the patient at a later date when valuable time has been lost, or worse, the patient discovers the diagnosis from another source other than the physician who is treating him, in the patient's mind the honesty of the treating physician is henceforth suspect, even though the patient may feel that the physician withheld information "in his best interests." Concealment makes palliative treatment more difficult: The patient may feel that more vigorous or no treatment is indicated or that very little treatment is indicated.

While on the subject of diagnoses, I think that the internist is especially valuable when he is looking for the trace symptoms of occult disease. We use these terms of "trace" and "occult" in the thought that any common disease may be detected early when only vague symptoms of malaise are present. It is especially the internist's responsibility to detect uncommon diseases, the diseases of "rare and exotic plumage," by an assiduous assay of early symptoms. The internist can only find such diseases by painstakingly and skillfully looking for them. It goes almost without saying that through early detection some diseases, such as cancer, may be removed and cured. In other instances one may hope not to cure the disease but to give additional time for the patient to arrange his life not only for himself but as it affects his family. In certain of the collagenous diseases early detection may mean an extension of the span of life of the patient so that he may be useful for a long period of time and even for an average normal statistical life span.

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In making diagnoses it is very important not to rely solely on laboratory or physical evidence. One or the other may be misleading at times; for instance, "peptic ulcers" 'seen' on X-ray examination sometimes do not exist.

The internist should have an essentially optimistic approach to the practice of medicine. A good physician resists the tendency "to throw up his hands" in hopelessness as to diagnosis, treatment, and prognosis. There is always at least a chance for a limited period of relief even though it may be only days or weeks, and at least one can give the patient the opportunity of preparing successfully for another and more fruitful life. This is not to say that heroic therapy or heroic diagnostic procedures out of all proportion to the seriousness of a disease or the gravity of the prognosis should be heedlessly indulged, but appropriate measures with at least some palliative hope are justifiable.

In this matter of diagnosis, therapy and treatment, economics must inevitably be a factor, and the internist must be resourceful. The indication for diagnostic and therapeutic procedures must be the need of the patient and not whether the patient can afford them. By administrative resourcefulness, certainly the vast majority of indicated diagnostic or therapeutic procedures can be carried out. The internist must take charge of facilitating the care of the patient as well as making the diagnosis and directing the treatment of the patient.

It is important to the internist to develop knowledge of and professional rapport with other specialists who may aid him in a diagnosis. Inherent in this is mutual respect for consultants in all specialty fields. In his own field, why would an internist want another internist to see his patient? It is because one internist cannot hope to know all of the complex facets of the specialty of internal medicine. In fact the subdivisions of internal medicine, namely, cardiology, chest diseases, gastroenterology, allergy, etc., indicate that some internists have special information in one facet of internal medicine. The internist who knows this about his associates and avails himself of consultation helps his patients.

The physician is charged with the responsibility of preventive medicine for the individual patient as much as he is charged with the treatment of the actual disease. The physician is charged with maintaining the individual efficiency of the patient as long as it is possible. He does not prevent death in the absolute sense but merely postpones death to the point where the maximum efficiency in the utilization of life has been obtained for the patient. The internist endeavors to maintain the parabolic curve of an individual's life so that he prepares himself for death, as a servant of God for the accounting which he must eventually give. In the last analysis the internist is a medical adviser who counsels his patients in the maximum utilization of their lives. In doing this he may be called in at any point of the patient's life and he should accept full advisory responsibility for the welfare of the patient during his lifetime.

A good physician does not allow himself to be frozen into a style and pattern of treatment which, while superficially effective and not attracting criticism, may not be maximally effective. Patterns which have proved to be less effective than newer additions to the medical armamentarium should be abandoned. One must strive constantly for an intellectual attitude toward every medical detail. Attention must be called to the fact that in many medical areas, diagnostically and therapeutically, there is a good armamentarium known for years but not utilized. I would point to proctoscopy as a procedure which should be a routine part of every physical examination. Doing "routine physical examination" one must constantly be alert. One must drive one's self in the practice of medicine to do certain procedures which are repetitive and yield only normal findings usually but which are a necessary part of the practice of medicine.

It is my opinion that while great advances are being made in medicine, in many instances we have very adequate treatments for the alleviation or cure of disease which are not being completely exercised because they require meticulous attention to detail along with constant supervision of the patient. The rheumatologic diseases are outstanding examples of this.

Both the psyche and the soma must be treated in the necessary amounts required to achieve, insofar as possible, a cure or sense of well-being, since the soma has created psychic change, and the reverse is also true.

# Communication

HUGH H. HUSSEY, M.D., F.A.C.P.*

PROPERLY USED, communication is man's most valuable asset. It affords a means of getting along with fellow men. Improperly or ineptly used, it is a source of misunderstanding or even disaster.

Doctors of medicine are, by title, teachers, and their teaching must be more than a mere dispensing of information. It must entail communication.

This is the distinction: Dispensing information is an action only by the informant. Communication is more than that; it also involves reaction by the recipient. Four elements are required, and this can best be illustrated by a story.

The story concerns a superintendent of the primary department in a Sunday school. A couple of times a year the curriculum of the school is interrupted by special services within the church. The interruptions take a good deal of planning. For one thing, the youngsters usually form a procession for moving from the school building into the church. They have to be carefully instructed about time of arrival, order of formation, how to march, where to sit in the church, and many other things.

One Sunday the superintendent was instructing her pupils about arrangements for a special service. As she stood before them, speaking slowly, simply, and distinctly, it was apparent that some were not attentive, and that was to be expected. There would be ways of taking care of it later. However, among the pupils in the very front row was a 6-year-older who was obviously "tuned in." The little girl gave every appearance of complete absorption in the teacher's words. As the talk ended, the superintendent gave the good teacher's usual parting shot: "Are there any questions?"

The attentive little girl in the front row put up her hand.

"Yes, Dorothy?"

"Is that a mink coat you're wearing?"

"No, Dorothy," was the reply, "It's muskrat."

The story demonstrates a chain of 4 elements in communication:

1. A sender—the teacher
2. A medium—the spoken message
3. A receiver—the pupil
4. The receiver's reaction (a message received and interpreted)

In the story the pupil did learn something, but it was not what the teacher intended. Was that a failure of communication?

It must be agreed that the last element in the chain—the learner's reaction—is most important. Hopefully, it will be something good for the receiver and his fellows and appropriate to the sender's intent.

### Causes of Failures

*Faults of the sender.* Once there was a physician who claimed he could cure cancer by giving injections of a compound of secret formula. He wrote about good results. He talked to patients about his methods. He even advertised his cure for cancer on the radio. A woman who heard one of the radio broadcasts had noticed a lump in one breast. She went to see the doctor who told her she had come just in time and that she did indeed have a cancer of the breast. He gave her a series of injections. After the fifth or sixth treatment she believed that the lump in her breast was smaller, and the doctor encouraged her in that belief. Later she died of cancer of the breast.

Knowing how humble most physicians are in talking about their ability to cope with cancer, it might be argued that the woman in the story was at fault. As a receiver of information she was too gullible. That may be partly so, but physicians will reject that argument. The source of trouble was the doctor—the sender of false information.

There would be no trouble at all if every physician could say "yes" to one question: "In the light of experience, reason, and God's revelations, am I an honest man?" Few people can say an unqualified "yes." However, the closer a physician comes in all particulars to saying "yes," the better.

(Honesty in its full sense does not countenance ignorance. The man who talks dogmatically from inadequate data cannot claim to be honest. However, to avoid belaboring that point and digressing into "statementship," the question can be given a corollary: "Do I know?")

*Failures in the act of teaching—The Message.* Examples of failure in a teacher's actions come readily to mind and are mainly technical defects. There are the poor delivery of a speaker or the ineffective writing of an author; distractions created by the teacher himself; delivery of information in a form incomprehensible for those intended to receive it. In that last category, all teachers—and science teachers in particular—are beset by the dangers of jargon and gobbledegook. Some who attempt to teach can never seem able to put their thoughts into forms that are understandable.

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*Failures of reception.* Then there were 3 English gentlemen riding in the same compartment of a train—all of them somewhat deaf. As the train approached a town, one of the men looked out the window and said, "It's Wembley."

"No it isn't," said the second, "It's Thursday."

"So am I," said the third, "Let's get a drink."

That story exemplifies the simplest type of failure in a receiver. He cannot get the message. This may happen because the message has been sent in the wrong form (in the story, any one of the several messages might have been received if it had been written instead of spoken), or, rarely, because the receiver lacks the capacity to receive any message (an intellectual failure).

Other causes of failure of reception include:

*Inattentiveness.* For instance, in spite of my best sending efforts, reverie has overtaken some of my readers. They should not feel guilty; they cannot hope to pick up every message that is sent their way.

*Jamming.* Two messages of opposite meaning arrive simultaneously. This phenomenon is especially prevalent during an election year.

*Distractions.* For all the clarity of a message when it is sent, it may not be received if there is too much static.

*Too many messages.* This is another and an inevitable intellectual failure. The human mind has its limitations as a receiver of information.

*Failures because of the learner's reaction.* Some time ago, at a meeting of a Roman Catholic society, the Archbishop of Washington introduced a friend of his, an eminent Episcopal clergyman. Speaking of the Episcopalian, the Archbishop said, "He left the rectorship of his church to fight Communism."

When the formal part of the meeting was over and people were standing around in small groups, it was apparent that the Archbishop's statement had meant different things to different people. There were those who supposed that the Episcopal minister was dismissed from a rectorship because of his political views. Others contended that the Archbishop had obviously meant to imply that the Episcopalian had joined the Roman Catholic Church. Still others understood that he had resigned in order to carry on a crusade against Communism.

Here were 3 reactions—all different. Why? The reason is self-evident. A learner's reaction is quite an individual interpretation, inevitably influenced by his personal motivations and objectives.

## Suggested Remedies

Most of my suggestions apply more or less directly to the physician as a teacher. For himself there must be constant effort to master his own thoughts—this in behalf of honesty. He must feel and express good will. Most important of all, he must be devoted to God.

The teacher's techniques must be sharpened so that he sends his message quickly and understandably. In that connection, there should be some way to provide special encouragement for people who have the rare talent for digesting, summarizing, simplifying, and delivering information uncovered by others.

The good teacher is always humble about his efforts. He knows that he cannot change the would-be learner. He can only present the opportunities for the learner to change himself by finding new goals in the light of his daily experiences. The teacher knows that learning is influenced by personal needs, and he can take advantage of that fact. For example, physicians and others are striving constantly to teach how to prevent accidents. The best learners are the people who have just had an accident. It is then that they have a personal need and become motivated to learn. The skillful teacher can often create that sense of need artificially.

## Conclusion

Obviously this essay has been an effort at education. I have written of teachers and learners as though they are separate groups. Actually they are not. They are all the same people. Because, you see, teachers are first and always learners.

Learning is a search for truth. That search is made difficult by the complexities of modern life. It is made easier by meditation—the attempt quietly to control the mind so that it seeks honestly for enlightenment.

Recently, one of the best teachers I know said that we have traded meditation for materialism. If that is so, let's reverse the trade. Let's loosen schedules and lighten pressures, to allow time for meditation in the daily schedule of living.

# Ruptured Cavernous Hemangioma of the Liver

## Report of a Case*

SAMUEL DESSOFF, M.D., F.A.C.P.†

It is usually not difficult to determine which system of the body is the origin of acute blood loss. Occasionally it may be difficult to pinpoint the exact area, but the search is at least narrowed. The following case seen recently on my service at Providence Hospital was something of a mystery and I believe worth reporting.

### Report of Case

The patient (H. M. P.), a Negro male aged 53, was admitted to the emergency room about 3 a.m. on December 16, 1966 because of several syncopal attacks during the night. After the first episode, which occurred in the bathroom, his wife helped him back to bed, and soon after that he had a convulsive episode. Incontinence occurred during these episodes, and he expectorated a large blood clot. He did not perspire and did not complain of pain. In the emergency room there were 2 episodes of clonic convulsive movements with loss of consciousness lasting about 3 minutes. He was sedated with Sodium Luminal,® given oxygen and intravenous glucose, and admitted to the Hospital.

In 1943 he had been operated on for an abdominal mass which he stated had been diagnosed as a granuloma Other than this he had been in exceptionally good health and usually took no drugs. There had been no hospitalization since 1943. About a week before this illness he had an upper respiratory infection for which he took 2 Anacin® tablets 4 times a day for 3 days. He drank very moderately and did not smoke. There was nothing significant in his family history. His wife stated that for about a year there had been some change in his personality and she felt that he had a definite mental disturbance. He had become irritable, accusing, and even paranoic.

On physical examination he was conscious and in no discomfort. He appeared pale but did not complain of weakness. The fundi were negative, the blood pressure 120/80, the pulse 84 and regular, and the respiratory rate 18. There were no enlarged lymph nodes. The lungs were clear to percussion and auscultation. The heart sounds were of good quality; no murmurs were noted, and there were occasional premature contractions. The abdomen was obese, and there was a right lower quadrant T-shaped scar. No masses or tenderness were noted. The liver and spleen could not be felt. The lower extremities were normal. No edema was found, and there were good pulses in the feet. Neurologic examination was normal.

The hemoglobin was 8.8 Gm., with a hematocrit of 30. The white blood cells numbered 15,000, with 64 per cent segmented forms, 3 per cent band forms, and 33 per cent lymphocytes. A urinalysis was normal. The serum urea nitrogen was 22 mg., serum $CO_2$ content, 29 mEq./L; serum potassium, 3.6 mEq./L; serum sodium, 139 mg.; serum bilirubin, 0.8 mg.; serum alkaline phosphatase, 5 units; serum cholesterol, 206 mg.; serum creatinine 1.3 mg.; and serum uric acid, 7.8 mg. The spinal fluid contained 16 erythrocytes and 4 lymphocytes per cu. cm., with chloride 125 mEq./L, glucose 90 mg., and protein 28 mg. Culture of the spinal fluid was negative. Bone marrow examination showed a normocytic anemia with mild plasmacytosis.

The patient was transfused on December 17, 18 and 23, 2,000 c.c. of blood being given. On December 16 the hemoglobin was 9.1 Gm., on the 17th 8.2 Gm., on the 22nd 8.2 Gm., and on the 26th 8.2 Gm. The platelet counts were 174,000 and 230,000; bleeding, coagulation and prothrombin times were normal. Total serum proteins were 7.4 Gm. with a normal A-G ratio; plasma electrophoresis was normal. Stool examinations were negative for blood. X-ray films of the skull, chest, and complete gastrointestinal series, including barium enema, were normal. The liver and spleen were remarkably well visualized and suggested that Thorotrast® had been used at some time (figure 1). A brain scan was normal. An electrocardiogram revealed only ventricular premature contractions. VDRL was nonreactive. A urine culture was negative.

The patient was examined on numerous occasions on the ward and always seemed cheerful and uncomplaining. At no time did he state that there was any discomfort. He ate well and was up and about freely. I saw him the morning before he died, and it was his belief that he was well and could go home. Examination at that time showed nothing of significance. The abdomen was soft and not tender, and no masses were felt. Early the next morning when the nurse came in to take his temperature he was found to be moribund and died before any treatment could be started, death occurring 12 days after admission.

This was a case of severe anemia, almost certainly due to bleeding, which did not improve after the transfusion of 2,000 c.c. of blood, indicating that the blood loss was continuing, with a complete lack of symptoms except for convulsions at the onset which were probably due to sudden cerebral anoxia.

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Necropsy revealed 2,000 c.c of bloody fluid in the peritoneal cavity; a large ruptured hemangioma occupying most of the right lobe of the liver, which weighed 1,430 Gm. (normal—1,500–1,800); and a soft spleen weighing only 30 Gm. (normal—150–200), with atrophic follicles and pulp. Microscopic sections of the liver showed a cavernous hemangioma and diffuse seeding of Thorotrast in the Kupffer cells. Those of the spleen showed chronic perisplenitis and Thorotrast deposits. Other intra-abdominal organs were normal.

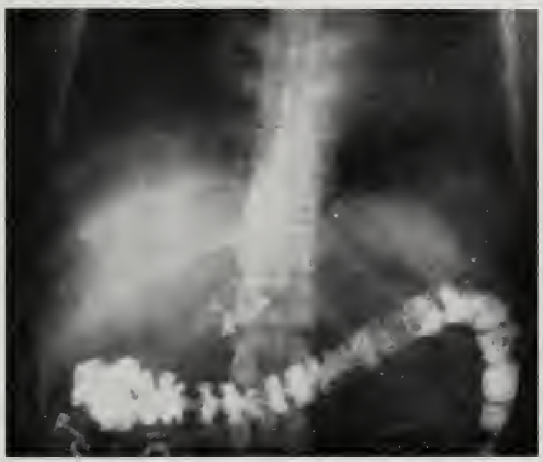

**FIG. 1. The presence of Thorotrast is easily seen in a very small spleen and in a liver which is reduced in size. Several lymph nodes are also noted.**

## Discussion

Henson, Gray and Dockerty[1] found 35 hemangiomas of the liver in surgical exploration of the abdomen between 1907 and 1954 and stated that hemangiomas are more common in the liver than in other internal organs and are usually cavernous in type. Hemangiomas belong to a group of tumors of the liver without hepatic elements. They rarely produce symptoms and may vary from pea-size to very large tumors. Hemorrhage occurs rarely. In the Jewish Hospital in Brooklyn, in 2,940 autopsies over a 10-year period, 17 cases were found. In almost all cases reported in the literature an abdominal mass was noted on examination and the diagnosis was usually made at surgery. Most patients were asymptomatic. Hepatic function was usually normal. Most tumors were found incidentally at surgery.

In this case it is probable that there was an injury at home which precipitated the first fainting spell. The syncopal episode was in all likelihood due to a brisk hemorrhage of brief duration and was later followed by slow oozing of blood. It is remarkable that there were no signs of peritoneal irritation. The abdomen was always soft, not tender, and masses were never noted.

There is another interesting finding that suggests some answer for the very small spleen and for a liver which was smaller than normal, when one would have expected a much larger liver. The deposit of Thorotrast in the liver with the history of surgery for a granuloma in 1943 indicates the presence of radioactive material for some 23 years. I shall remind you that thorium dioxide was used for visualization of the liver and spleen in the early thirties. It was later found that the material remained in these organs for many years. The excretion rate was extremely slow, with some eventual deposits in the lymphatics being noted. William Looney, working in the Radioisotope Laboratory of the U. S. Naval Hospital, reported that the biological half-life of Thorotrast is estimated to be 400 years.[2] He further stated that Thorotrast was present in the tissues as long as 19 years in patients he studied. The spleen was most vulnerable with destruction of the architecture, fibrosis, and marked shrinking. Some of the spleens he studied were one-fifth normal size.

It is my belief that in our case the long-continued radiation effected the reduction in the size of the liver. One can conjecture that in the absence of the Thorotrast effect, and in the presence of a right upper quadrant mass, which is the usual finding in cavernous hemangiomas, surgery might have resulted in recovery.

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PRESCRIBING INFORMATION. For complete information consult Official Package Circular. *Indications:* Infections of respiratory, gastrointestinal and genitourinary tracts and skin and soft tissues due to tetracycline-sensitive organisms, in patients with increased susceptibility to monilial infections. *Contraindications:* The drug is contraindicated in patients hypersensitive to its components. *Warnings:* Photodynamic reactions have been produced by tetracyclines. Natural and artificial sunlight should be avoided during therapy. Stop treatment if skin discomfort occurs. With renal impairment, systemic accumulation and hepatotoxicity may occur. In this situation, lower doses should be used. Tooth staining and enamel hypoplasia may be induced during tooth development (last trimester of pregnancy, neonatal period and childhood). *Precautions:* Bacterial superinfections may occur. Infants may develop increased intracranial pressure with bulging fontanels. In gonorrheal therapy, serologic tests for syphilis should be conducted initially and monthly for 3 months. *Adverse Reactions:* Glossitis, stomatitis, nausea, diarrhea, flatulence, proctitis, vaginitis, dermatitis, and allergic reactions may occur. *Usual Adult Dosage:* 1 capsule q.i.d. Continue for 10 days in Beta-hemolytic streptococcal infections. Administer one hour before or two hours after meals. *Supplied:* Capsules, bottles of 16 and 100. Each capsule contains tetracycline phosphate complex equivalent to 250 mg. tetracycline HCl activity and 250,000 units of nystatin. For Oral Suspension, 125 mg. tetracycline and 125,000 u. nystatin/5 ml., 60 ml. bottles.

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**Night Leg Cramps** . . . Unwelcome Bedfellow
In Diabetes,[1] Arthritis,[2] and Peripheral Vascular Disorders[2]

**now . . . specific therapy for night leg cramps**

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Consistently effective, QUINAMM provided complete relief in 94% of 200 patients studied, many of whom were severe cases refractory to other medication.[3] Your prescription for one tablet at bedtime often controls painful night cramps with the initial dose . . . helps restore restful sleep.

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**Prescribing Information: Composition:** Each white, beveled, compressed tablet contains: Quinine Sulfate 260 mg. and Aminophylline 195 mg. **Contraindication:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Precautions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets. **References:** 1. Shuman, C.: Am. J. Med. Sci., 225:54, 1953. 2. Perchuk, E., et al.: Angiology, 12:102, 1961. 3. Rawls, W., et al.: Med. Times, 87:818, 1959. 6/67 Q-706A

# even in ulcerative colitis...

characterized by:
- diarrhea, cramps, tenesmus
- bloody, mucoid, purulent stools

# LOMOTIL® tablets/liquid

Each tablet and each 5 cc. of liquid contains:
diphenoxylate hydrochloride . . . . 2.5 mg.
(Warning: May be habit forming)
atropine sulfate . . . . . . . . . . . . 0.025 mg.

# controls diarrhea

In six published studies[1-6] detailed results are given on the use of Lomotil in 111 patients with chronic ulcerative colitis. They show that Lomotil gave satisfactory to "excellent" control of diarrhea in more than two-thirds of these patients. As the disorder advances and destroys bowel musculature, the motility-lowering action of Lomotil, understandably, has less effect.

The successful use of Lomotil in a disorder as exceedingly difficult to treat as moderate ulcerative colitis emphasizes again its unsurpassed antidiarrheal effectiveness in these more common conditions:

- **Gastroenteritis**
- **Acute infections**
- **Spastic colon**
- **Drug induced diarrhea**
- **Functional hypermotility**

---

*For correct therapeutic effect*
*Rx correct therapeutic dosage*

*sage:* The recommended initial daily doses, given in divided doses until diarrhea is ntrolled, are:

*ildren: Total Daily Dosage*

| | |
|---|---|
| 3-6 mo. . . | ½ tsp.*t.i.d. (3 mg.) |
| 6-12 mo. . | ½ tsp. q.i.d. (4 mg.) |
| 1-2 yr. . . . | ½ tsp. 5 times daily (5 mg.) |
| 2-5 yr. . . . | 1 tsp. t.i.d. (6 mg.) |
| 5-8 yr. . . . | 1 tsp. q.i.d. (8 mg.) |
| 8-12 yr. . . | 1 tsp. 5 times daily (10 mg.) |
| *Adults:* | 2 tsp. 5 times daily (20 mg.)<br>or 2 tablets q.i.d. |

*Based on 4 cc. per teaspoonful.

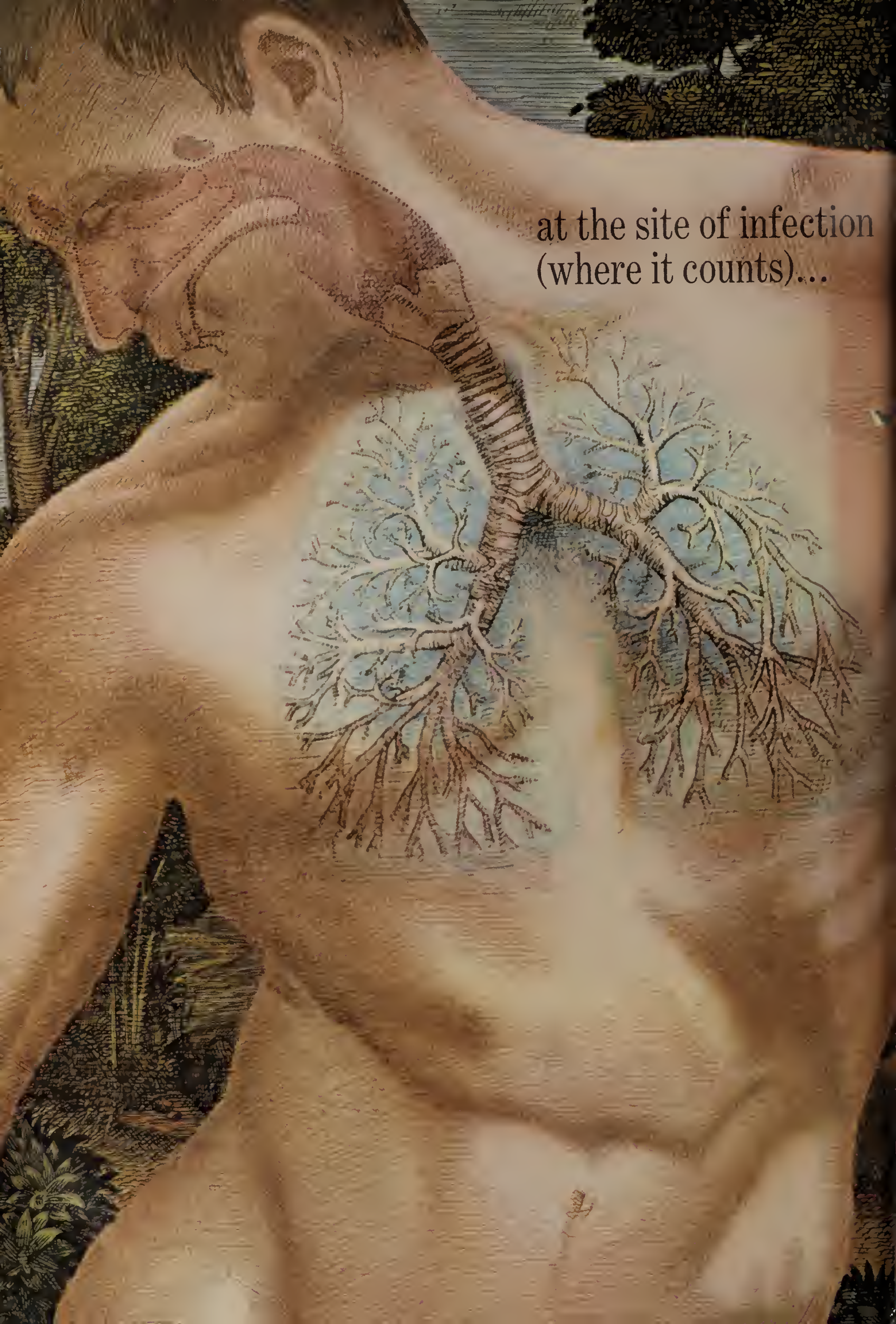
Maintenance dosage may be as low as one-fourth the initial daily dosage.

*Precautions:* Lomotil is a federally exempt narcotic preparation of very low addictive potential. Recommended dosages should not be exceeded, and medication should be kept out of reach of children. Should accidental overdosage occur signs may include severe respiratory depression, flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and tachycardia. Lomotil should be used with caution in patients with impaired liver function or those taking addicting drugs or barbiturates.

*Side Effects:* Side effects are relatively uncommon but among those reported are gastrointestinal irritation, sedation, dizziness, cutaneous manifestations, restlessness, insomnia, numbness of the extremities, headache, blurring of vision, swelling of the gums, euphoria, depression and general malaise.

1. Barowsky, H., and Schwartz, S. A.: J.A.M.A. *180:*1058-1061 (June 23) 1962. 2. Cayer, D., and Sohmer, M. F.: N. Carolina Med. J. *22:*600-604 (Dec.) 1961. 3. Hock, C. W.: J. Med. Ass. Georgia *50:*485-488 (Oct.) 1961. 4. Van Derstappen, G., and Vandenbroucke, G.: Med. Klin. *56:*962-964 (June 2) 1961. 5. Merlo, M., and Brown, C. H.: Amer. J. Gastroent. *34:*625-630 (Dec.) 1960. 6. Weingarten, B.; Weiss, J., and Simon, M.: Amer. J. Gastroent. *35:*628-633 (June) 1961.

**SEARLE** *Research in the Service of Medicine*


at the site of infection
(where it counts)...

# Ilosone® provides more antibacterial activity than any other oral erythromycin

**Acid stable, better absorbed... Ilosone produces faster, higher, more prolonged blood levels, even in the presence of food[1-3]**

Because it is the most active form of oral erythromycin, Ilosone can help assure consistently greater antibacterial activity at the site of infection. Ilosone produces peak antibacterial blood levels two to four times those of other erythromycin preparations.[1,2] Not only are these levels attained earlier, but they are maintained for much longer periods. Even the presence of food does not seem to affect the activity of Ilosone.[1,3]

In the treatment of patients with bacterial infections susceptible to erythromycin, Ilosone has compiled an excellent therapeutic record. Since it exerts its greatest activity against gram-positive organisms, it is particularly useful in common respiratory and soft-tissue bacterial infections. Ilosone kills—not merely inhibits—streptococci, pneumococci, and more strains of staphylococci than any other macrolide antibiotic. This bactericidal action, coupled with the high antibacterial levels attained, makes Ilosone especially valuable in patients with low host resistance, such as infants, debilitated individuals, and diabetics.

Ilosone has shown no cross-resistance with penicillin and may be effective against organisms that have become resistant to that agent. Despite its high antibacterial activity, Ilosone has demonstrated a low incidence of side reactions. Blood dyscrasias, ototoxicity, and tooth staining have not been observed. Infrequent cases of drug idiosyncrasy, manifested by a cholestatic jaundice, have occurred, but there have been no known definite residual effects.

**Now available:**
New! Ready-mixed Ilosone Liquid 125! (Contains erythromycin estolate equivalent to 125 mg. erythromycin base per 5-cc. teaspoonful.)

700970

**Ilosone®**
**Erythromycin Estolate**

Lilly

*(See next page for prescribing information.)*

# Ilosone®/the most active oral form of erythromycin

**Description:** Ilosone is the most active form of oral erythromycin that has been developed. Because it is stable in acid, well absorbed, and excreted in lesser amounts in the bile, it provides faster, higher, and longer-lasting levels of antibacterial activity (ABA) in the serum, even when taken with food, than do comparable doses of erythromycin.

**Indications:** Ilosone is indicated in infections caused by microorganisms sensitive to its action (especially staphylococci, hemolytic streptococci, and pneumococci). The drug is therefore useful in a high proportion of bacterial diseases encountered in clinical practice and particularly in the treatment of bacterial infections of the upper and lower respiratory tract and soft tissues.

In the treatment of acute bacterial pharyngitis and tonsillitis, this antibiotic has promptly eradicated the bacteria (streptococci) and has produced a parallel prompt clinical improvement. There have been no group A beta-hemolytic streptococci resistant to this preparation. In beta-hemolytic streptococcus infections, treatment should be maintained for ten days to prevent the development of rheumatic fever or glomerulonephritis.

Erythromycin estolate has proved to be very effective in pneumococcus pneumonia and in acute bronchitis with pneumococci on culture. Bronchopneumonia and otitis media in children have responded well to its use.

The antibiotic has been used very successfully in staphylococcus infections. Good therapeutic results have been obtained in soft-tissue infections, abscesses, cellulitis, carbuncles, wound infections, and furunculosis.

In serious staphylococcus infections, erythromycin preparations should be used only in combination therapy with other antimicrobial agents. As is the case with any treatment regimen used in these severe conditions, surgical procedures should be performed when indicated, and large dosages of the antimicrobial agents should be employed. In this fashion, Ilosone has been effective in staphylococcus pneumonia, osteomyelitis, septicemia, empyema, and meningitis.

Multiple 500-mg. doses of the drug have also been useful in gonorrhea and syphilis. Since penicillin is the drug of choice for the treatment of syphilis and gonorrhea, erythromycin estolate should be employed for these infections only in patients with a history of penicillin allergy. Also, other infections due to susceptible bacteria in patients known to be hypersensitive to penicillin or other antibiotics may be considered for treatment with Ilosone.

**Contraindications: Ilosone is contraindicated in patients with a known history of sensitivity to this drug and in those with preexisting liver disease or dysfunction.**

**Adverse Reactions:** Data obtained from seven years' use of propionyl erythromycin ester and erythromycin estolate (Ilosone) indicate that hepatic dysfunction with or without clinical jaundice may occur during or following courses of therapy with the drug.

Changes in liver function tests in such cases have been indicative of intrahepatic cholestasis. The symptoms appear to be the result of a form of sensitization. The initial symptoms have developed in some cases after a few days of treatment but generally have followed one or two weeks of continuous therapy or several courses of the drug. Symptoms reappear promptly, usually within forty-eight hours, if the drug is readministered to sensitive patients. Eosinophilia was noted in peripheral blood counts. The findings readily subsided without apparent residual effects when treatment was discontinued. Recovery was delayed in one reported instance. The physician indicated in this case that either drug-induced jaundice or viral hepatitis may have been responsible for the findings.

In one clinical study involving ninety-three patients treated with the antibiotic, three cases of jaundice were observed and an additional eleven cases developed some changes in liver function tests. Three of the patients had abnormal liver function tests a second time on readministration of the drug.

Even though it is assumed that not all cases of jaundice have been reported, it seems clear that the number is small compared with the amount of drug that has been used. Reported cases have included persons in whom there had been administered other drugs known to be associated at times with hepatic side-effects and cases in which the presence of viral hepatitis or other disease may have been responsible for the findings. In some of the cases, associated gastro-intestinal symptoms simulated the colic of biliary tract disease. In other instances, clinical symptoms and results of liver function tests resembled findings in extrahepatic obstructive jaundice. It appears that the occurrence of jaundice after administration of Ilosone is infrequent, but further investigations are being made to estimate its incidence more accurately.

In those cases mentioned above in which jaundice appeared be definitely related to use of the drug, laboratory findings we characterized by increased direct-reacting bilirubin, eleva alkaline phosphatase levels, negative or weakly positive cephal flocculation and thymol turbidity tests, elevated serum gluta oxalacetic transaminase levels, peripheral eosinophilia, and n mal cholecystograms.

Individual idiosyncrasy seems evident since jaundice has been reported in other patients taking prolonged courses of medication. Patients with chronic infection have been given 1 to 2 Gm. of the drug daily for periods of two to six months, a patients with rheumatic fever have taken prophylactic doses 0.5 Gm. daily for two years without difficulty. In one group 144 patients who received the drug daily for two years, no jau dice was noted. It was of interest that members of six of th patients' families, who were not taking the drug, had episo of jaundice during the study period.

Transaminase and serum alkaline phosphatase levels we determined in a group of fifty-four adults and children who to 250 mg. of Ilosone daily for an average of sixteen months rheumatic fever prophylaxis. The results were compared w those of a similar group of forty-four patients who received pe icillin. There were no cases of jaundice in either group. Elevati of SGPT and serum alkaline phosphatase levels during the cou of treatment was observed in one patient treated with Ilos and in two patients treated with penicillin. Seven other patie in the group receiving Ilosone and four others in the penicil group showed elevations in one of the tests at some time duri administration of the drugs.

Very satisfactory therapeutic results, without toxicity, we reported in 102 pediatric patients who received short-term (te day) courses of Ilosone in the treatment of streptococcus inf tions. Results of liver function tests in these patients we comparable to those in a similar control group who had recei penicillin.

Gastro-intestinal disturbances not associated with hepatic fects are observed in a small proportion of individuals as a res of a local stimulating effect of the medication on the alimenta tract; however, the normal intestinal gram-negative bacter flora is not appreciably altered by erythromycin drugs.

Although allergic manifestations are uncommon with the u of erythromycin, there have been occasional reports of urtica skin eruptions, and, on rare occasions, anaphylaxis.

**Administration and Dosage:** Ilosone is administered orally.

Ilosone Pulvules®, Ilosone Liquid 125, Ilosone, 125, for O Suspension, Ilosone Drops, Ilosone Chewable Tablets.

For infants and for children under twenty-five pounds of b weight, the usual dosage is 5 mg. per pound every six hours; children twenty-five to fifty pounds, 125 mg. every six hou (Tablets Ilosone Chewable should be chewed or crushed a swallowed with water.)

For adults and for children over fifty pounds, the usual dos of Ilosone is 250 mg. every six hours.

For severe infections, these dosages may be doubled.

When larger doses are indicated, parenteral erythrom therapy should be considered.

In the treatment of syphilis, the recommended total dosag 20 to 30 Gm. given in divided doses for a period of ten to fift days. Close follow-up of the patient is necessary since eryth mycin drugs have not had adequate evaluation in all stages syphilis. Examinations of spinal fluid are recommended as p of the follow-up therapy.

For gonorrhea, 500 mg. four times a day for four days recommended. In the treatment of gonorrhea, patients wit suspected lesion of syphilis should have a dark-field examinat before receiving antibiotics, and monthly serologic tests sho be made for a period of three months.

**How Supplied:** Pulvules Ilosone, Capsules, N.F., 125 and 250 (equivalent to base), in bottles of 24 and 100.

Ilosone Liquid 125, Oral Suspension, U.S.P., 125 mg. (equival to base) per 5-cc. teaspoonful, in 60-cc. and pint-size packa

Ilosone, 125, for Oral Suspension, N.F., 125 mg. (equival to base) per 5-cc. teaspoonful, in 60 and 150-cc.-size packa

Ilosone Drops, 5 mg. (equivalent to base) per drop, in 10-cc. packages, with dropper calibrated at 25 and 50 mg.

Tablets Ilosone Chewable, N.F., 125 mg. (equivalent to ba in bottles of 50. [032

*References:* 1. Griffith, R. S., and Black, H. R.: Am. J. M. Sc., *247*:69, 1 2. Griffith, R. S., and Black, H. R.: Antibiotics & Chemother., *12*:398, 3. Hirsch, H. A., Pryles, C. V., and Finland, M.: Am. J. M. Sc., *239*:198, 1960.

*Additional information available to physicians upon request.*
*Eli Lilly and Company, Indianapolis, Indiana 46206.*

# PRESIDENT'S PAGE

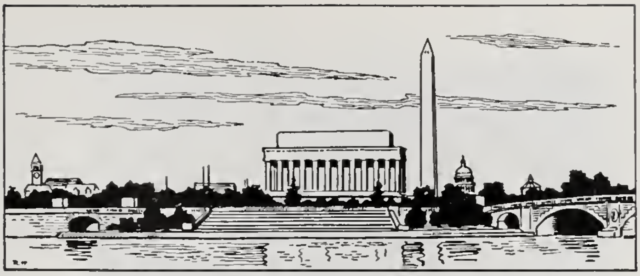
## WELL DONE, DR. YATER

THE DEDICATION OF THIS ISSUE OF THE MEDICAL ANNALS OF THE DISTRICT OF COLUMBIA to Dr. Wallace M. Yater is an inadequate recognition of the years of selfless service rendered to our organization by a truly remarkable individual. Dr. Yater has given thousands of hours in quiet but persistent efforts to raise the level of quality and to improve the professional and community service of the Medical Society of the District of Columbia. His own professional and scientific history is reported elsewhere in this issue. Because of his unassuming manner his untiring service to this Society has hitherto been little appreciated by the members at large and his efficient execution of a wide variety of functions has been given little publicity.

Dr. Yater has been Editor of this journal for 35 years; its excellence is a continuing tribute to his ability in this sphere. He has served as President of the Medical Society, member and later Chairman of its Executive Board, and member or chairman of many of our important committees. His calm approach with impartial judgment has assisted in the solution of many problems. His capacity in administrative and economic matters in addition to his professional excellence reflects a versatility of talent seldom encountered in a man of science. The local community and Society have Dr. Yater to thank for many benefits. Praise he does not seek, nor thanks, though both are due. We hope that this YATER NUMBER of the ANNALS will convey to him in some small way our deep appreciation of his years of productive effort. We wish him good health and happiness in continuing activity, for he would never be content in a passive state. To Dr. Wallace Mason Yater—"Well done—a good and faithful servant."

Henry D. Ecker

WALLACE MASON YATER, M.D.
Editor of the Medical Annals of the District of Columbia since its inception in 1932



# EDITORIALS

## Wallace Mason Yater—His Life

Dr. Wallace Mason Yater has been a member of the Medical Society of the District of Columbia since 1923 and has taken an active role in many of its activities. He was President of the Society in 1952 and has been Editor of the Medical Annals since he founded this publication in January 1932.

Dr. Yater proposed the need for a Medical Society publication to publish papers by its members and to bring this scientific material to the city and country at large. News material of special interest to the membership was included to maintain its basic tie with the profession in Washington.

Dr. Yater's original publication, which began with a distribution to 800 members, is now one of the outstanding state medical society journals in the country, with a circulation of 3,100 copies throughout the United States and many foreign countries. His editorial ability, devotion and energy through years of duty have made the Annals a most valuable adjunct to the Medical Society of the District of Columbia. It gives living testimony to his truly great service.

In recognition of this fact the Executive Board of the Society has authorized that this edition of the Annals be dedicated to Dr. Yater. The articles have been prepared by physicians trained by him. Their respect, appreciation and gratitude to him are reflected in their work.

Dr. Yater was born in Canton, New York, and later moved with his parents to Washington, D. C., where he was educated in the public schools. He received his B.A. degree cum laude from George Washington University in 1917 and an M.D. degree from Georgetown University School of Medicine in 1921.

Dr. Yater's internships were served at Garfield Memorial Hospital and Georgetown University Hospital. In 1922 he entered general practice and concurrently served on the faculty of Georgetown University School of Medicine until 1926 as: Instructor in Surgical Anatomy, Instructor in Physical Diagnosis, and Professor of Physical Diagnosis. During this time he completed his first book, "Symptom Diagnosis," in collaboration with Dr. Wilfred M. Barton. In 1926 he joined the Mayo Clinic as a Fellow in Medicine. He received an M.S. degree in Medicine from the University of Minnesota in 1928.

In 1929 Dr. Yater returned to Georgetown as the first full-time Clinical Professor in the history of the Medical School. He immediately improved the curriculum by bringing to Georgetown such outstanding teachers as Dr. Jacob Markowitz as Professor of Physiology. Dr. Yater with Dr. Markowitz and a team of surgeons at the Mayo Clinic were the first to transplant the heart in experimental animals. He established fellowships in medicine at Georgetown, and these led to the postgraduate education of scores of physicians well-trained in internal medicine. It is this group of physicians, taught and trained by Dr. Yater, practicing medicine throughout the country that has been his most satisfying accomplishment.

From 1929 to 1930 Dr. Yater was Associate Professor of Medicine at Georgetown and in 1930 he became Professor and Director of the Department, which position he held until October 1945. He was also Chief of Medicine at Gallinger Municipal Hospital (now D. C. General Hospital) from 1932 to 1945.

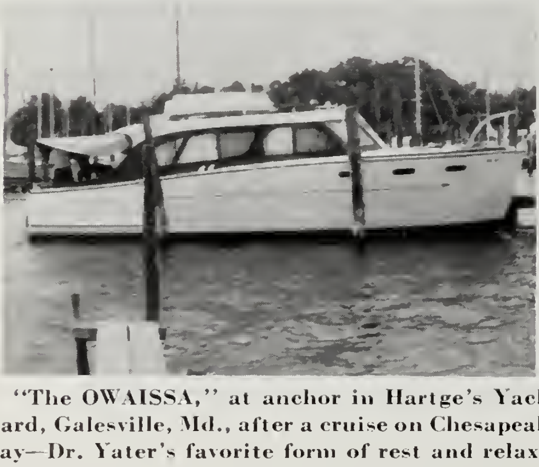
In 1932 he was married to the former Ruth Millicent Becker. They have 4 children: Mrs. Millicent Howard, Stephanie, Wallace J., and Mrs. Camille Stanley.

During World War I Dr. Yater served in the Student Army Training Corps as First Sergeant of his company. Upon graduation from medical school he became First Lieutenant in the Army Medical Reserve Corps. During World War II he was Civilian Consultant to the Medical Department of the Army and Walter Reed General Hospital and a member of the Committee on

**WALLACE AND MILLICENT YATER as they appeared in 1954.**

Cardiovascular Diseases of the National Advisory Health Council of the U. S. Public Health Service. He is a consultant to the Clinical Center of the National Institutes of Health.

Dr. Yater has been active in many national scientific organizations. He served as Governor of the American College of Physicians for 15 years and Regent of the College for 6 years; he was elected Secretary General of the organization in April 1956 and continues to hold that post. He is a diplomate of the American Board of Internal Medicine. He is also past Chairman of the Section on Experimental Medicine and Therapeutics of the American Medical Association, past Chairman of the Section for the Study of Peripheral Circulation of the American Heart Association, a former Director of the latter Association, and Associate Editor of *Circulation.*



**"The OWAISSA," at anchor in Hartge's Yacht Yard, Galesville, Md., after a cruise on Chesapeake Bay—Dr. Yater's favorite form of rest and relaxation.**

His memberships include the American Medical Association, the Southern Medical Association, the American Society of Internal Medicine, the American Heart Association, the Washington Heart Association, the Academy of Medicine of Washington, D. C., and Sigma Chi. He is a retired member of the American Society for Clinical Investigation.

Dr. Yater was founder of the American Association of Medical Clinics and was its first President. He was also a member of the founding group of the American Society of Internal Medicine and a member of its first Board of Trustees.

**DR. YATER aboard his cruiser with 2 of his grandchildren, John and Barbara Howard.**

Dr. Yater has presented papers at many medical meetings throughout the country. He gave the Kober Lecture at Georgetown in 1938 and the Mayo Foundation Lecture in 1942. He has published 2 textbooks, "Symptom Diagnosis" and "The Fundamentals of Internal Medicine," which are used extensively throughout the United States and abroad. He is the author of 145 published articles on medical subjects, mainly original contributions to the medical literature. In addition to his pioneer work on the heart, Dr. Yater was one of the first investigators to report on the use of contrast arteriography and venography.

Following retirement as Professor of Medicine at Georgetown University School of Medicine in 1945, Dr. Yater organized a diagnostic and treatment center, the Yater Clinic, located at 1780 Massachusetts Avenue, N.W., Washington, D. C. The Yater Clinic has thrived under his active directorship. The patient contact of such importance to him is now realized to its fullest there. His teaching and practice combine an inimitable balance of laboratory and clinical examination of the patient, capable use of clinical observation, proper regard for therapeutic indication, responsibility to the patient, and respect for the dignity of the person. His students, residents and fellow physicians have always been impressed by his logical, informed mind, at its best in discussion of cases in clinical conferences. His amazing knowledge, personal and intellectual integrity, and dedication to duty have been and still are an inspiration to those who know him. Dr. Yater identifies with medicine as physician, teacher, scientist, author, and clinical investigator.

Stephen W. Nealon, Jr., M.D.
*Guest Editor*

# Dr. Yater—An Appraisal by His Fellows

"During my many years of practice—private, institutional, tropical, and within the United States—in internal medicine there is one factor which stands out above all else. That is the excellent training I received in this field as a student under Dr. Yater, during a postgraduate fellowship under his direction, and through association with him in one way or another during my years of practice in Washington. While quite a few of the physicians with whom I have worked and fraternized oftentimes had difficulty with diagnosis and therapy, I must say I have avoided many problems, which I attribute to the unique approach taught by Dr. Yater. I have known many fine internists throughout the world and consider Dr. Yater far superior to the great majority.

"Dr. Yater, in addition to being an excellent teacher, has been an outstanding contributor, through numerous publications, to the field of medicine and to humanity in general."

L. M. Drennan, Jr., M.D.

"One of the most significant events of my life occurred late in the fall of 1928, when as an intern at Georgetown University Hospital I first met Wallace Yater. He had just returned from his studies at the Mayo Clinic and was in the near future to become Professor of Medicine at Georgetown University Medical School.

"He began to make daily ward rounds, and I was impressed with the logic and clarity of his discussions. His knowledge of medicine was profound and a revelation to those of us who were in his audience. Through his influence I received a Fellowship in Medicine at Georgetown and my career in internal medicine was launched.

"During Dr. Yater's stay at Georgetown he began to modernize the Medical Department. He invited outstanding medical men for grand rounds, and I vividly remember Emanuel Libman, of bacterial endocarditis fame, for his keen and witty observations.

"A magazine club was organized and continued for years by the fellows and former fellows. Clinical pathologic conferences were started both at Georgetown University Hospital and what is now District of Columbia General Hospital.

"Dr. Yater would work interminable hours, and I remember how frequently we would be going across the street to Teehans for a snack at 10 or 11 o'clock at night. The Chief never seemed in a hurry, but somehow he was able to do more work than any person I have ever known. His numerous articles and the positions he has held in national societies attest to his ability and accomplishments. The men who worked with him have always held him in high esteem and over the years have invariably addressed him as 'Dr. Yater' and not as 'Wallace'—a mark of their high respect for him.

"It is my sincere belief that the coming of Dr. Yater to Georgetown marked the beginning of the rise to eminence among medical schools which it has achieved.

"Personally, I owe Dr. Yater a debt of gratitude for having influenced me and for having given me training which I have never forgotten. At the age of 70 he is still the clear thinking, thorough clinician of my youth, and I hope he stays this way for many more productive years."

Samuel Dessoff, M.D.

"In a given time, in the milieu in which he found himself, Wallace Mason Yater has become a superb clinician, investigator, educator, and administrator; Dr. Yater's achievements are difficult to equal and hard to excel. In keeping with the Oath, I affirm that I look upon him who taught me even as one of my own parents. Whatever good I may accomplish will considerably reflect my years spent under Dr. Yater's tutelage. In the review I have written for this issue those of us who have been Yater students will recognize that it is based on a familiar outline."

William J. Martin, M.D.

"I was associated with Dr. Yater as a fellow in medicine while at Georgetown University in 1944 and 1945. He is an extraordinary man dedicated to the continued improvement of the practice of medicine.

"I should like to mention an experience with an interesting diagnostic problem that turned up during my period of service as a medical resident at the D. C. General Hospital (known in those days as Gallinger Municipal Hospital).

"Dr. T. F. Keliher was my 'attending' at the time and we presented this case to Dr. Yater at one of his well-known weekly seminars.

"As I remember it, the patient had obstructive jaundice with chills and fever. The possibility of the existence of a fistula between the duodenum and common bile duct due to obstruction from either a stone or neoplasm of the head of the pancreas was discussed in detail without coming up with any definitive answer.

"A few days later Dr. Keliher contacted me by phone to say that Dr. Yater had phoned him long distance from an out-of-town medical meeting suggesting that the G.I. series be repeated with films taken every 30 minutes.

"This procedure was done and resulted in a beautiful demonstration of the intrahepatic biliary tree that was almost completely filled with barium along with a dilated fistulous connection between the duodenum and the biliary system (see D. C. Annals, March 1945).

"My purpose here is to exemplify the remarkable dedication of Dr. Yater to the improvement of the scientific medical knowledge of all who had the opportunity to be associated with him."

James M. Moser, Jr., M.D.

"I was delighted to hear of the special issue of the Annals which will be dedicated to Dr. Yater in recognition of his service as editor.

"I should like to relate an anecdote involving his handling of a case when I was serving as one of his fellows. This experience demonstrates his dogged thoroughness and sharp acuity in diagnosis.

"I was a newly appointed fellow when a patient in the hospital was referred to Dr. Yater for consultation. Dr. Yater asked me to do a good history and physical on the patient prior to his visit. The patient was a white male, aged 55, and an old TB; he had been coughing for a number of years but had begun to go downhill without adequate demonstrable cause. There were no other significant items in the history. Aside from a few scattered rales on both sides of the chest, the physical examination was not remarkable other than the presence of some hemorrhoids. I had intended to do a rectal but, because of the patient's complaint of pain, the examination was unsatisfactory. X-ray of the chest had previously indicated what appeared to be a 'healed or healing' miliary form of TB or perhaps silicosis.

"On reporting these findings to Dr. Yater he immediately took the cue. He took me over to X-ray to look at this 'miliary TB' and then promptly marched me up to the patient's bedside again. He informed me that he was going to perform a rectal in the proper manner. This he did, much to the consternation of and only over the violent objection of the patient. It gave him the answer—CA of the prostate with pulmonary metastases. 'Scheele,' he said, 'always do a *complete* physical.' He then directed me to perform a rectal on this patient when the patient was more tolerant and feeling a little better.

"Unfortunately, the patient's condition regressed rapidly and he expired without my performing the rectal.

"Did Scheele ever do the rectal as Yater had directed? Yes—'in the morgue.' When Dr. Yater was informed that the patient had died he called me in and told me that they could not get an autopsy. Since I had not been able to palpate the lesion in vivo he gently hinted that I had better get down to the morgue and take this last opportunity to become acquainted with this pathology.

"Lesson learned: All good Yater Fellows must do rectals when performing physicals, *especially* on all patients having hemorrhoids.

"This experience taught me a very valuable lesson and certainly brings out Dr. Yater's incomparable knack for thoroughness under all circumstances, no matter how adverse. This thoroughness, coupled with his keen mind and fine background of knowledge, has contributed immeasurably to the high stature which he has attained within the medical profession."

A. F. Scheele, M.D.

## Fellows and Trainees of Dr. Yater

During his years at Georgetown as Head of the Department of Medicine Dr. Yater initiated the training of Fellows in Internal Medicine. Fifty-two young men came under his teaching program. Most of them are engaged in active practive; 3 have died; all of them have contributed in many ways to the furtherance of medical progress. To the literature they have contributed, as author or co-author, 41 books and 718 articles. However, this is only a partial record. Listed here are the names of Dr. Yater's Fellows and the positions they now occupy in addition to their private practice.

Milton Alvis, M.D., in practice of internal medicine in San Antonio, Texas.

James F. Ambury, M.D., Assistant Clinical Professor of Medicine, George Washington University School of Medicine.

Joseph M. Barker, M.D. (deceased), practiced cardiology in Beverly Hills, Calif.; formerly on the staff of the Yater Clinic, Associate Professor of Clinical Medicine and Director of Heart Station, Georgetown University Medical Center.

Walter Berberich, M.D., Chief of Medicine and Cardiology, Latrobe Hospital, Latrobe, Pa.; Consultant in Internal Medicine, McGinnis Hospital, Ligonier, Pa.; Consultant in Cardiology, Torrance State Hospital, Torrance, Pa.

Joseph E. Brackley, M.D., Consultant in Medicine to Stony Brook Retreat, Keene, Calif.; in practice of internal medicine in Bakersfield, Calif.

John R. Cavanagh, M.D., Senior Attending in Psychiatry, Washington (D. C.) Hospital Center.

Julius D. Damian, M.D., in practice of surgery in Washington, D. C.

John A. Dattoli, M.D., Camp Hill, Pa.

Samuel Dessoff, M.D., Associate Physician, Providence Hospital, Washington, D. C.; Consultant in Cardiology, Glenn Dale Hospital, Glenn Dale, Md.

Robert H. Detwiler, M.D., Attending Pediatrician, Arlington (Va.) Hospital; Clinical Instructor in Pediatrics, Georgetown University School of Medicine.

Leo I. Donovan, M.D., in general practice in Bethesda, Md.

Lawrence M. Drennan, Jr., M.D., Medical Director, United Fruit Company, New Orleans, La.

Richard P. Fitzgerald, M.D., in practice of internal medicine in Harrisburg, Pa.

William D. Foote, M.D., Chairman, Department of Ophthalmology, Washington (D. C.) Hospital Center; Assistant Professor of Ophthalmology, Georgetown University School of Medicine.

Benjamin Golden, M.D., in practice of surgery in Washington, D. C.

Henry B. Gwynn, M.D., in practice of internal medicine in Mobile, Ala.

Francis P. Hannan, M.D., in general practice in Washington, D. C.

Hugh H. Hussey, M.D., Director, Division of Scientific Activities, American Medical Association; formerly Dean and Chairman, Department of Medicine, Georgetown University School of Medicine.

Sol Katz, M.D., Chief of Medical Service, Veterans Administration Hospital, Washington, D. C.; Professor of Medicine, Georgetown University School of Medicine; Special Lecturer on Pulmonary Disease, George Washington University School of Medicine.

James A. Kehoe, M.D., Clinical Assistant Professor of Medicine, Georgetown University School of Medicine.

Thomas F. Keliher, M.D., Professor of Medicine and Director of Diagnostic Clinic, Georgetown University Medical Center.

Robert T. Kelley, M.D., Clinical Associate Professor of Medicine, Georgetown University School of Medicine.

Joseph P. Kenrick, M.D., in general practice in Chevy Chase, Md.

Ralph A. Kilby, M.D., U. S. Army Hospital, Fort Jackson, S. C.

William C. Lambert, M.D., in general practice in Washington, D. C.

James M. Loftus, M.D., in general practice in Washington, D. C.

Joseph J. McCarthy, Jr. M.D., Clinical Instructor in Medicine, Georgetown University School of Medicine.

Michael J. McInerney, M.D. (deceased), Clinical Associate Professor of Medicine, Georgetown University School of Medicine; Chief of Medicine, Georgetown and Providence Hospitals.

John M. Maloney, M.D., in practice of internal medicine in Springfield, Mass.

William J. Martin, M.D., Consultant in Medicine, Mayo Clinic and Mayo Foundation; Associate Professor of Medicine, Mayo Graduate School, University of Minnesota, Rochester, Minn.

Thomas W. Mattingly, M.D. (Brigadier General, M.C., U.S.A., Ret.), Coördinator, Regional Medical Program of Metropolitan Washington; Clinical Professor of Medicine, Georgetown and George Washington University Schools of Medicine; Consultant in Cardiology to Walter Reed General, Children's and Holy Cross Hospitals and Washington Hospital Center; formerly Chief, Department of Medicine, Walter Reed General Hospital.

Richard H. Meredith, M.D., Deputy Medical Director, U. S. Civil Service Commission, Washington, D. C.

James M. Moser, Jr., M.D., Medical Officer, Food and Drug Administration.

Stephen W. Nealon, Jr., M.D., Associate Clinical Professor of Medicine, Georgetown University School of Medicine; Editor, *The Georgetown Medical Bulletin.*

Bernard E. Nunez, M.D. Associate Clinical Professor of Medicine, Georgetown University School of Medicine.

William F. Oliver, M.D., Assistant Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles.

Lawrence M. Pack, M.D., in general practice in Arlington, Va.

**DR. YATER in a characteristic lecture pose.**

Hyman W. Paley, M.D., Director, Cardiopulmonary Division, Mount Zion Hospital and Medical Center, San Francisco; Assistant Clinical Professor of Medicine and Consultant to Cardiovascular Research Institute, University of California School of Medicine, San Francisco.

Thomas J. Ready, M.D., Administrator, Veterans Administration Hospital, Washington, D. C.

Isadore Rodis, M.D., Clinical Associate Professor of Psychiatry, Georgetown University School of Medicine; Senior Attending Staff, Washington (D. C.) Hospital Center.

Robert C. Rush, M.D., Clinical Assistant Professor of Orthopedic Surgery, Georgetown University School of Medicine.

William T. Saccardi, M.D., in practice of internal medicine in Washington, D. C.

Bertram F. Schaefer, M.D., Clinical Associate Professor of Medicine, Georgetown University School of Medicine.

Andrew F. Scheele, M.D., Director, Region 6, Virginia State Department of Health; Consulting Staff, Prince William Hospital, Manassas, Va.

Vincent J. Seiwert, M.D., Associate Professor, University of Cincinnati College of Medicine; Director, Isotope Laboratory, St. Mary's Hospital, Cincinnati.

John F. Stapleton, M.D., Medical Director, Georgetown University Hospital, and Associate Dean, Georgetown University School of Medicine; formerly Associate Professor of Medicine and Chief of the Division of Cardiology, Woman's Medical College of Pennsylvania.

Hugh L. C. Stevens III, M.D., in clinic practice in Nashville, Tenn.

F. Daniel Suttenfield, M.D. (deceased), Hampshire Memorial Hospital, Romney, West Va.; Past National Surgeon, Reserve Officers Association of the United States.

J. Lawn Thompson, Jr., M.D., Associate Clinical Professor of Medicine, Georgetown University School of Medicine; Senior Attending Physician, Washington (D. C.) Hospital Center.

Gerald M. Tierney, M.D., Clinical Instructor in Medicine, Georgetown University School of Medicine.

Joseph J. Wallace, M.D., Clinical Associate Professor of Medicine, Georgetown University School of Medicine.

Paul P. Welsh, M.D., Chief of Medicine, St. Jerome Hospital, Batavia, N. Y.

# DON'T JUST SIT AROUND ESCHEWING THE FAT.

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You'll be joining the ranks of professionals who believe overweight is one health hazard that can be reduced.

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That's what prompted preparation of research-tested scientific diets which are offered to you free. They're a realistic balance of the 4 food groups—meat, bread and cereals, fruits and vegetables and dairy foods. They're diets you'd write yourself, if you had the time.

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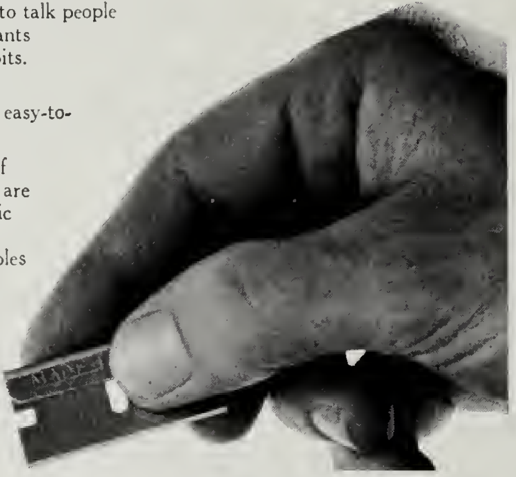

Send me the Project Weight Watch kit of materials including diets.

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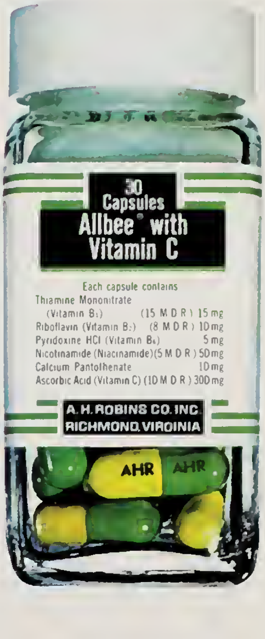
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| hyoscyamine sulfate | 0.1037 mg. | 0.3111 mg. |
| atropine sulfate | 0.0194 mg. | 0.0582 mg. |
| hysocine hydrobromide | 0.0065 mg. | 0.0195 mg. |
| phenobarbital | (¼ gr.) 16.2 mg. | (¾ gr.) 48.6 mg. |
| (Warning: may be habit forming) | | |

*Brief summary.* Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Administer with caution to patients with incipient glaucoma or urinary bladder neck obstruction. Contraindicated in acute glaucoma, advanced renal or hepatic disease or a hypersensitivity to any of the ingredients.

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# Question of the Month—?

**More and more patients are using non-Governmental hospital outpatient facilities. What do you believe is causing this trend?**

### Answers and Comments

Herbert S. Gates, M.D. (Obstetrics-Gynecology): Some years ago the majority of doctors had their office and home in the same building. This arrangement made the physician accessible to the patient at all times in case of sudden illness or emergency. Today most doctors reside away from their offices.

In many cases of injury, overdose or accidental taking of a toxic or poisonous drug, acute cardiac episodes, and other emergencies, a fully equipped and staffed emergency room is necessary and patients are "rushed" to these facilities where adequate emergency care can be rapidly initiated.

On the other hand, the emergency facilities are abused by patients who have been injured or ill for several days and go to the emergency suite deliberately to evade their doctor. Many of these people think that services are free at these areas and are severely shocked when told the amount of the bill for services rendered.

We must not forget that some doctors do not care to be disturbed after their long day is ended, or on holidays, days off and weekends.

Robert H. Parrott, M.D. (Hospital Administration): I am not aware that the added use of outpatient facilities is at non-Governmental hospitals to the exclusion of Government hospitals, and I rather doubt that this is so. However, most hospitals with emergency room facilities and outpatient facilities are seeing more and more patients. Several factors interrelate:

1. Some patients believe that there is greater availability of these services in the hospital than in the physician's office. There are, in fact, some physicians who encourage the use of such facilities by their patients on nights and weekends. Some patients assume (correctly or incorrectly) that a physician would prefer not to be disturbed at night or on a weekend.
2. Some patients assume, often incorrectly, that the cost of a hospital emergency room visit will be less than an emergency call from a physician. Sometimes they are in effect correct because of the restrictions of certain hospitalization and health insurance plans.
3. Certain patients' use of hospital outpatient facilities rather than an individual physician is a reflection of medical indigency which is closely combined with location of the city and race. Under current circumstances, physicians' offices are not able to absorb the extraordinary cost of providing care for medically indigent patients whereas many hospitals feel that they have the moral obligation to do so. There are not sufficient physicians in the areas of the city which contain the largest proportion of medically indigent patients, who in this city are primarily Negro.
4. Some patients may get the idea that the hospital outpatient department represents a distillate of all of the "wonderful" facilities that most hospitals have. This is, of course, only an illusion at the firing line level where the patient is seen in the emergency room by a house officer or, in some instances, a hired licensed physician often no more experienced than the patient's own physician.

The upshot of all of this is often discontent and less than ideal medical care. The emergency room in outpatient departments is overcrowded with patients who do not really represent emergency needs and/or who are not properly the responsibility of the hospital. The conscientious practicing physician loses the thread of continuity in the care of his patient. Patients often become exercised over the amount of waiting necessary in hospital clinics and the fact that they frequently are examined by a house officer.

The solution could come through increased coöperation of physicians to cover each other's practice, better distribution of physicians, perhaps through special group clinics in certain parts of the city, increased public information programs on the function of hospital emergency rooms, and better distribution of reimbursement for medically indigent care through a Title XIX program.

Edward W. Nicklas, M.D. (Internal Medicine): I believe the reason for the trend of patients to utilize more and more hospital outpatient facilities is primarily due to the tendency of physicians to refer them there when it is inconvenient to see them, or when the doctor is unavailable with no other physician willing to "cover."

Another reason for patients utilizing these facilities is that, in most cases, the visits can be paid for by insurance carriers, because they are usually considered as emergencies and patients would not otherwise be reimbursed under their insurance coverage. I could not estimate the number who would be influenced in this way, but I am sure that it would be statistically important.

I think that there is another growing group of patients who are consciously or subconsciously following an impression which will grow more and more important in the future; i.e., if hospitals are good places in which to be sick, then they must be good places to go to find out what is wrong with them. I think I remember an article by Leo Brown (of the AMA) expounding on this belief, about a year or two ago, and the article was most interesting.

James E. Fitzgerald, M.D. (Internal Medicine): More and more the hospital is becoming, in the minds of people, the medical center for the community. This is at least in part a reflection of the depersonalization of medical practice. It is understandable on this basis that both physicians and patients will make increasing use of ancillary services such as laboratory and X-ray. In addition, the trend of hospitals to staff emergency rooms with full-time physicians provides patients with readily available emergency service and relieves the hard-pressed physician of one of the more burdensome aspects of practice.

**If any members have dissenting views, your Editorial Staff will be pleased to receive and publish them.**

## AMA Policy on Recruitment of Medical Students, Interns, and Residents

On the basis of the recommendations of the Ad Hoc Committee on Residency Appointment Dates, plus consultation with representatives of numerous other organizations, the Council on Medical Education of the American Medical Association submitted the following report, adopted by the House of Delegates in November, 1966.

**Medical Students.** The Council believes that it is in the interests of neither hospital training programs nor future residents for medical students to be required to commit themselves to residencies in specific specialties as early as 2 years prior to graduation from medical school, before they have had any opportunity for effective exposure to most medical specialties, and before they have begun their internships.

It is recommended to the House of Delegates that:

1. The practice of seeking commitment of medical students, prior to graduation, to residencies in specific specialties be condemned as coercive and restrictive of the students' rights, and

2. It is the position of the AMA that special commitments on the part of medical students merely reflect the students' intentions at the time they were made, and are neither legally nor ethically enforceable as contracts. Students should assume such training in medical specialties or general practice as they feel is consistent with their personal circumstances and interests. The freedom to chart one's future is as sacred as the physician's freedom to choose his patients or the patient's freedom to choose his doctor.

**Interns.** The Council notes that the competition between interns for residency appointments and the concurrent competition between residency program directors for trainees have resulted in a trend toward residency appointments so early in the intern year that the candidate has little or no opportunity to select his field of specialty training on the basis of his experience as an intern. While it is impractical to expect deferral of residency appointments until after completion of the entire internship, it is highly desirable that those interns who have not already identified their areas of specialty interest be given opportunity for further exploration during at least the first 4 months of the internship.

It is recommended to the House of Delegates that:

1. The Council on Medical Education enlist the coöperation of all appropriate specialty groups for the voluntary establishment of a uniform date for appointment of interns to first-year residencies, and that this date be set not earlier than approximately November 15.

2. The significance of the uniform date for appointment of interns to first-year residencies is that the intern is not obligated to accept an ap-

pointment, even though it is offered, before the date voluntarily agreed upon by the responsible program directors in each specialty.

3. In developing a method for implementing a program of uniform appointment, interested specialty groups should consider the experience of intern program directors prior to establishment of the National Intern Matching Program, Inc., as well as the experience of the psychiatry program directors prior to development of their own matching program.

4. If the establishment of uniform appointment dates by additional specialty groups results in the creation of additional residency matching plans, the resources of the NIMP should be explored; furthermore, a reorganization of the NIMP should be considered, if necessary, in order to make this effective organization more broadly useful in the area of its special competence, and to eliminate the confusion which might arise from the existence of multiple, independent matching operations.

5. If additional residency matching programs are developed, the Directory of Approved Internships and Residencies should serve to list the matching code number for residencies just as it now does for internships.

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# Health Dept. Notes

## Nursing in D. C. Department of Public Health

The role of the public health nurse has changed considerably during the past century. In addition to the traditionally accepted functions of the profession, nurses now are involved in program planning, coördination of medical services, individual and group therapy, and health counseling. Nurses provide a link of continuity essential to good health care.

Nurses actively participate in epidemiological investigations and consultations in a variety of programs in hospitals, homes, and other agencies in the District of Columbia.

There has been a continual expansion of nursing activities. Recently, a nurse clinical specialist in mental health was assigned to the Court of General Sessions to act as liaison between the Health Department's alcoholism program and the courts. In addition, a nurse was assigned to coordinate a discharge and referral planning program at the D.C. General Hospital.

A variety of training programs has been developed for sub-professionals working under the direction of a nurse. In this way nursing assistants and aides are employed to extend the professional services of the nurses.

When the nursing service was first initiated within the D.C. Department of Public Health in 1935, there were some 3 dozen public health nurses on the staff. Today, there are 1,835 nursing personnel in the Department, including D.C. General and Glenn Dale Hospitals.

The primary goals of the Bureau of Nursing are: to provide nursing service to all program areas of the D.C. Department of Public Health; to develop standards of nursing care; to provide leadership in the Department as well as the community in initiating new and innovative techniques; and to implement staffing patterns and effective utilization of all nursing personnel. Nurses are assigned to work in homes, schools, clinics, mental health centers, and D.C. General and Glenn Dale Hospitals.

The nursing service of the D.C. Department of Public Health utilizes nurses from all categories of basic education programs in teaching, supervision, and other clinical specialty areas.

For providing the essential nursing services within the District of Columbia the Bureau of Nursing is operating on a budget of almost 4 million dollars.

The Department's Bureau of Nursing is composed of the Divisions of Public Health Nursing, Mental Health Nursing, Clinic Nursing, and Inspections and Standards.

The tasks of the Division of Public Health Nursing include the care of sick and injured patients, prevention of disease, rehabilitation and health instruction.

Mental health nurses work with patients in the Mental Health Centers operated by the Department and in the patients' homes; they also assist in the care of patients with emotional problems.

Clinic nurses provide professional support for the patient-care team in the numerous clinics of the D.C. Department of Public Health.

The Inspections and Standards Division is concerned with nursing care given by hospitals, nursing homes and other similar places, with responsibility for legal standards and enforcement.

Our nursing staff works with others in the Department to prevent disease and prolong life.

Murray Grant, M.D., D.P.H.
*D.C. Director of Public Health*

# Tissue's healing nicely. Yet anxiety slows his steps toward recovery.

By helping overcome anxiety and tension which can thwart the convalescent's progress, EQUANIL (meprobamate) often may play an important role in medical and surgical aftercare.

**Cautions:** Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use may result in dependence or habituation in susceptible persons—as ex-addicts, alcoholics, severe psychoneurotics. After prolonged high dosage, drug should be withdrawn gradually to avoid possibly severe withdrawal reactions including epileptiform seizures. Side effects include drowsiness and, rarely, allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute non-thrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. If an allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Warn patients of possible reduced alcohol tolerance. Should drowsiness, ataxia, or visual disturbances occur, dose should be reduced. If symptoms persist, patients should not operate vehicles or dangerous machinery. A few cases of leucopenia, usually transient, have been reported following prolonged dosage. Other blood dyscrasias—aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia—have occurred rarely, almost always in the presence of known toxic agents. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. Prescribe very cautiously for patients with suicidal tendencies. Suicidal attempts should be treated with immediate gastric lavage and appropriate supportive therapy.

**Contraindications:** History of sensitivity to meprobamate.

**Composition:** Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

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# DOCPAC Briefs

## or Is Your Professional Future Worth Political Involvement?

ARE YOU CONCERNED about your professional future in a political world? Would you like better representation in Congress of views consistent with freedom to practice medicine without increasing regulation by the Federal Government? ARE YOU CONCERNED with the need for providing physicians, their wives, and medical allies, such as dentists, nurses, technicians, etc., with an opportunity to assume a more effective and a more active role in public affairs?

DO YOU HAVE AN "OPEN MIND" as to who shall decide which patients you may see, what your fee shall be, which drugs you may prescribe, and what method you will use in billing your patients? ARE YOU "OPEN-MINDED" to the suggestion that you are mainly concerned with collecting your fee and no longer are dedicated to the welfare and special needs of your patients? I doubt it.

For better or worse, this is an organized world. Unless the people in the healing arts professions speak with one voice, the time will arrive (and it is later than you think) when we shall all be employees of a massive controlling government. Abilities, initiative, the will and desire to be of service to our fellow man will be a lost cause. Each day control inches a bit forward. You are required to complete a few more forms, hire a few more employees to keep Government records, and lose a little more control and responsibility for your own professional affairs.

DO YOU BELIEVE that the medical profession and its medical allies owe it to themselves and to the public to stand up strongly for the values of individual choice and voluntary organization as opposed to complete Federal domination of health care? DO YOU BELIEVE that electing members to the Congress who share our philosophy of self-determination, individual initiative, and competitive free enterprise is the only way to prove to ourselves and to the world that we are still a free, independent and compassionate people? DO YOU BELIEVE AS RESIDENTS OF THE DISTRICT OF COLUMBIA and the surrounding Metropolitan Area that there is a vital need for a well-organized medical political action group to make its voice heard more effectively in civic affairs; that the next few years are critical in stemming the tide of welfarism in our country and our city?

If this is your philosophy you should be a member of DOCPAC, the District of Columbia Political Action Committee. DOCPAC is not affiliated with either major political party. It is not bound by Democratic or Republican party labels. Only the program, platform and philosophy of the candidate determine DOCPAC's support.

In the 1966 election DOCPAC gave directly to the campaign of a Democrat and a Republican on the House of Representatives District Committee. Both were reëlected. DOCPAC through its affiliation with the American Medical Political Action Committee supported 146 candidates—131 for the House of Representatives and 15 for the Senate. Eighty-five per cent of these candidates were elected. We are very proud of this degree of success.

Why not join DOCPAC and help develop an organization that can speak effectively for you and your profession, one that will help elect members of Congress who are interested in responsible, constructive and fiscally sound government. YOU are needed.

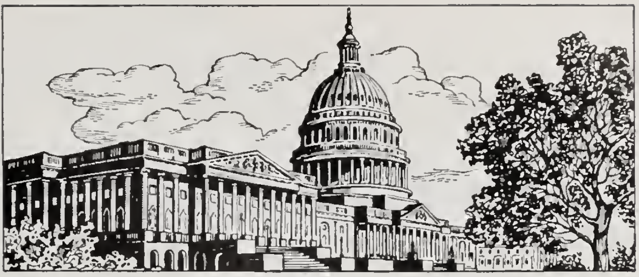
MRS. ANN RAPEE
*Vice Chairman, District of Columbia Political Action Committee*

## Drug Dependence

DRUG DEPENDENCE has a very important characteristic to remember. It is almost always a chronic relapsing disorder, and cycles of withdrawal and reversion to drug abuse are likely to occur in most cases. Success or failure of treatment, however, cannot be measured by the single criterion of relapse. Such factors as comfort with self, relations with others, and vocational adjustment must be considered. There is good reason to believe that the total course of the dependence is influenced by adequate treatment over rather long-range periods.

COMMITTEE ON PROBLEMS
OF DRUG DEPENDENCE
*Washington Psychiatric Society*

N.B. The Committee would appreciate it if members of the D. C. Medical Society will comment on or relate their experiences concerning problems of drug abuse or misuse.



# NEWS & PERSONALS

## Summary of Executive Board Actions

### Proceedings of June 26 Meeting

Dinner for the Board members was served at 6:40 p.m. in the Exhibit Hall of the Medical Society. Dr. Karl C. Corley, Chairman, presided at the meeting. Present were Drs. Frank S. Bacon, C. Willard Camalier, Jr., Robert J. Coffey, Henry D. Ecker, Raymond T. Holden, Margaret M. Kenrick, William S. McCune, Edward W. Nicklas, Paul R. Wilner, and Mr. George W. Cooley, Secretary. The meeting was called to order at 7:10 p.m.

The minutes of the June 5, 1967 meeting were approved as mailed.

**Committee Meetings:** The Secretary reported that the following committees had met since the last meeting of the Board:

June 6 Subcommittee on Regional Medical Programs
7 Fee Review Committee
8 Medical Bureau Committee
9 Committee on Rehabilitation and Chronic Illness
12 Committee on Liaison with Allied Professions
14 Committee on Liaison with the Clergy
14 Advisory Group on Regional Medical Programs
15 Traffic Committee
20 Committee on Alcoholism

**Board of Credentials:** The following actions were taken on recommendations made by the Board of Credentials:

*Associate Member*

Howard William Doan, American Medical Association, Chicago

*Transfer*

*Associate to Active:* Francis L. Land

**Medical-Dental Research Foundation:** A letter from Dr. Samuel Dove, Secretary of the Foundation, was read. The Medical-Dental Business Research Foundation, Inc. (first called the Medical-Dental Economic Bureau) was incorporated in August 1964. At that time the Medical Society of the District of Columbia appointed Dr. Myer Stolar to represent it on the Board of the Foundation for a period of 3 years as of July 1964. During this entire period Dr. Stolar has served as President of the organization and "his guidance has been invaluable." Dr. Dove recommended that the Board reappoint Dr. Stolar for another period of 3 years, beginning July 1967. This recommendation was accepted by the Board.

**Committee on Liaison with Allied Professions:** This Committee had met with representatives of the District of Columbia Nurses' Association, at its request, to consider a joint statement on "The Venipuncture and the Administration of Intravenous Fluids by Licensed Professional Nurses Practicing in the District of Columbia." The joint statement, agreed to by this Committee's representatives and the representatives of the nursing group, as well as representatives of the Hospital Council of the National Capital Area, Inc., was approved by the Board.

**ODMC Contract Renewal:** For the information of the Executive Board the Secretary reported that the Alexandria Medical Society, the Arlington County Medical Society, and the Fairfax County Medical Society had voted not to renew their contracts and that the Montgomery County Medical Society had taken no action (as of June 26). The Prince George's County Medical Society had voted to sign along with the Medical Society of the District of Columbia. The Secretary reported that conferences were being arranged with General Peatfield to discuss the contract renewal in accord with previous Executive Board action.

**Report on Meeting of AMA House of Delegates in Atlantic City, June 1967:** Drs. Holden and Camalier, the Society's delegates, reported in some detail on actions taken by the House of

Delegates. Both resolutions submitted by this Society had been acted upon favorably:

A. The report of the Committee on Human Reproduction, chaired by Dr. Holden, was approved by the House of Delegates with minor editorial changes.

The Board voted to approve and adopt this report of the AMA as a policy of the Medical Society of the District of Columbia. It was also suggested that this report be forwarded to the Society's Committee on Medicolegal Problems to determine whether or not any action should be taken in the way of proposed legislation for the District of Columbia.

B. In reference to the Disability Insurance Program, Dr. Camalier reported that almost all physicians speaking before the Reference Committee were in favor of continuing a program similar to the one now in operation. The House of Delegates approved a Program with the following 6 points:

1. Assurance that present members be considered and their present coverage be maintained.
2. That a contract for 5 years be negotiated with an insurance carrier, which would probably be the Firemen's Fund, since that was the only insurance carrier which seemed agreeable to maintaining the present contract for a 5-year period.
3. That all promotional literature be approved by the Board of Trustees of the AMA.
4. That a committee of the AMA maintain continuous review over the experiences of the Program.
5. That all doctors be notified and it be made perfectly clear to those who joined that this is a *term policy*.
6. That all operations of the Program be open to investigation by a committee of the AMA.

Dr. Holden and Dr. Camalier were commended for their report (see August issue of Medical Annals, page 482) and for successfully obtaining approval of the 2 resolutions submitted to the House of Delegates by this Society.

**Committee on Public Information and Education:** The following information was transmitted by the Secretary for the information of the Board:

*Community Health Week* to be held, October 15, 16, 17 and 18; tests for glaucoma, hearing, blood type (and possibly donor), and chest X-ray (mobile) to be sponsored by the Society during the week.

*150th Anniversary of the Society:* Brochure to be prepared covering the first 150 years, taken from previous histories and from records, members, etc.

**Committee on Aviation Medicine:** A proposal made by Dr. Robert S. Poole, Dr Clifton R. Brooks, and several others that a Committee on Aviation Medicine be created was approved.

### Other Business

1. It had been suggested that a questionnaire be sent to the membership to determine their interest in serving on a lecture series program at area Seminaries and Schools of Theology. Such a questionnaire was approved, to be sent to the membership with one of the mailings of the *Newsletter*.

2. Dr. Ecker reported that he had selected a chairman for the new Committee on Drug Addiction and that letters were now being sent to various organizations requesting that they name representatives to this Committee.

3. The Secretary reported on a request from Merck, Sharpe and Dohme in regard to co-sponsoring a seminar on the business side of medical practice sometime this fall. The Board agreed that the Secretary should discuss the matter further with representatives of the Company.

There being no further business, the meeting was adjourned.

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Individually Designed for Each Physician or
Partnership and Funded with Leading Mutual Funds
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District 7-1114

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announces

# a breakthrough in the control of pain

# Talwin®

brand of
**pentazocine**
(as lactate)

**a potent, injectable non-narcotic**

## For every physician who has ever prescribed morphine

Talwin is the new potent non-narcotic injectable analgesic which is indicated for relief of all types and degrees of pain in acute and chronic disorders. Talwin 30 mg. is usually as effective an analgesic as morphine 10 mg. or meperidine 75 to 100 mg., but needs no narcotics controls. The duration of action of Talwin may sometimes be less than that of morphine.

Talwin is relatively free from adverse effects o morphine, such as constipation, urinary retention or severe respiratory depression.

It has been used, in varying dosages, in ove 12,000 patients for relief of pain of medical dis orders, of active labor and postoperative pain also for preoperative or preanesthetic medication and as an adjunct to anesthesia.

---

A brochure incorporating analyzed information on Talwin is available. The completeness of the information will permit you to evaluate the role Talwin can play in your practice.

**You can depend on Talwin to relieve pain:**

**WHATEVER the intensity of the pain**
**the cause of the pain**
**the site* of the pain**
**the duration of the pain**
**the chronicity of the pain**
**the age† of the patient**

**Talwin does not require a narcotics prescription**

The World Health Organization Expert Committee o Dependence-Producing Drugs concluded that "...ther was no need at this time for narcotics control of penta zocine [Talwin] internationally or nationally." (*WH Tech. Rep. Ser.*, No. 343, 1966, p. 6.)

It is our sincere belief that the discovery of Talwin b Winthrop Laboratories will be of great value to you an your patients for whom you may have to prescribe potent analgesic.

*Talwin should not be used for patients with increased intracranial pressur head injury or pathologic brain conditions.

†Until sufficient experience is gained, it should not be administered to childre under 12 years of age.

# in digestive disorders:

*B and C vitamins aid therapy.* Nausea, vomiting, and severe diarrhea may seriously interfere with the digestion and absorption of nutrients. STRESSCAPS capsules, containing therapeutic quantities of vitamins B and C, may help meet the needs of these patients. In digestive disorders, as in many stress conditions, STRESSCAPS vitamins aid therapy.

**Stresscaps®**

Stress Formula Vitamins Lederle

FOR PROFESSIONAL RECOMMENDATION ONLY

Each capsule contains:

| | |
|---|---|
| Vitamin $B_1$ (as Thiamine Mononitrate) | 10 mg |
| Vitamin $B_2$ (Riboflavin) | 10 mg |
| Vitamin $B_6$ (Pyridoxine HCl) | 2 mg |
| Vitamin $B_{12}$ Crystalline | 4 mcgm |
| Vitamin C (Ascorbic Acid) | 300 mg |
| Niacinamide | 100 mg |
| Calcium Pantothenate | 20 mg |

Recommended intake: Adults, 1 capsule daily, for the treatment of vitamin deficiencies. Supplied in decorative "reminder" jars of 30 and 100; bottles of 500.

LEDERLE LABORATORIES, A Division of American Cyanamid Company, Pearl River, New York

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Lederle

STRESSCAPS

# alwin—brand of pentazocine (as lactate)

ontraindications: *Increased Intracranial Pressure, Head Injury, Pathologic Brain Conditions in which clouding of sensorium is ndesirable.* Talwin (brand of pentazocine) should not be adminis- red in these cases, since drug-induced sedation, dizziness, nausea, respiratory depression could be misleading.

ecautions: *Pregnancy.* No teratogenic or embryotoxic effects tributable to the use of Talwin have been seen in extensive repro- uctive studies in animals; however, like all new drugs, Talwin ould be given with caution to pregnant women. A large number patients in labor have received the drug with no adverse reac- ons other than those that occur with commonly used strong algesics. However, as with other strong analgesics, Talwin should used with caution in women delivering premature infants.

*nbulatory Patients.* Since sedation, dizziness, and occasional phoria have been noted, ambulatory patients should be warned t to operate machinery, drive cars, or unnecessarily expose them- ves to hazards.

*rtain Respiratory Conditions.* The possibility that Talwin (brand pentazocine) may cause respiratory depression should be con- lered in treatment of patients with bronchial asthma. Talwin and of pentazocine) should be administered only with caution d in low dosage to patients with respiratory depression (e.g., m other medication, uremia, or severe infection), obstructive piratory conditions, or cyanosis.

*tients Dependent on Narcotics.* Because Talwin is a narcotic- tagonist, patients dependent on narcotics and receiving Talwin ay occasionally experience certain withdrawal symptoms. Talwin ould be given with special caution to such patients. It has been served that some patients previously given narcotic-analgesics one month or longer had mild withdrawal symptoms when the ug was replaced with the analgesic, Talwin. After a short period adjustment the subjects were usually able and willing to con- ue taking Talwin, and relief of pain was satisfactory.

*naddicted Patients Receiving Narcotics.* Symptoms believed to indicative of antagonism to the opiate may be observed rarely h administration of Talwin to patients receiving opiates for a ort time. Intolerance or untoward reactions are seldom observed er administration of Talwin to patients who have received single ses or who have had limited exposure to narcotics.

*paired Renal or Hepatic Function.* Although laboratory tests ve not indicated that Talwin (brand of pentazocine) causes or reases renal or hepatic impairment, the drug should be adminis- ed with caution to patients with such impairment. Extensive er disease appears to predispose to greater side effects (e.g., rked apprehension, anxiety, dizziness, sleepiness) from the usual nical dose, and may be the result of decreased metabolism of the ug by the liver.

*ocardial Infarction.* As with all drugs, Talwin (brand of penta- ine) should be used with caution in patients with myocardial arction who have nausea or vomiting.

*iary Surgery.* Until further experience is gained with the effects Talwin on the sphincter of Oddi, the drug should be used with ution in patients about to undergo surgery of the biliary tract.

verse Effects: Talwin is relatively free from the undesirable side ects associated with morphine, such as constipation, urinary re- tion, or severe respiratory depression. Furthermore, Talwin duces less nausea, vomiting, and diaphoresis than meperidine.

over 12,000 patients who received Talwin intramuscularly, sub- aneously, or intravenously, nausea, the most frequent adverse ect, occurred in approximately 5.0 per cent. In decreasing order occurrence were vertigo, dizziness or lightheadedness; vomiting; l euphoria. Respiratory depression was reported as an adverse ction in 1.0 per cent.

e incidence of each of the other adverse effects was well below per cent: constipation, circulatory depression, diaphoresis, uri- y retention, alteration in mood (nervousness, apprehension, pression, floating feeling), hypertension, sting on injection, headache, dry mouth, flushed skin including plethora, altered uterine contractions during labor, dermatitis including pruritus, dreams, paresthesia, and dyspnea occurred rarely after administration of Talwin (brand of pentazocine). Furthermore, each of the following adverse reactions occurred in less than 0.1 per cent: tachycardia, visual disturbance (blurred vision, diplopia and nystagmus), hallucinations, disorientation, weakness or faintness, muscle tremor, chills, allergic reactions including edema of the face, taste alteration, insomnia, diarrhea, cramps, and miosis; laryngospasm in one patient.

Talwin has not produced severe respiratory embarrassment in adults (never apnea), even with large amounts. A small number of newborn infants whose mothers received Talwin during labor had transient apnea. The incidence of temporary diminution in the rate or strength of uterine contractions is low after administration of Talwin, similar to that following meperidine hydrochloride. (In reporting no interference with normal labor in patients receiving Talwin, one investigator further stated that the drug may increase uterine activity.) Generally, no significant fetal heart rate change occurs.

Laboratory tests of blood and of liver and kidney functions have revealed no significant abnormalities. A minimum and probably insignificant increase in the per cent of eosinophils in peripheral blood counts and bone marrow occurred occasionally.

Talwin is well tolerated by patients with diabetes mellitus, and no changes in insulin requirements have been observed.

Dosage and Administration: *Adults, Excluding Patients in Labor.* Average recommended single parenteral dose is 30 mg., by intramuscular, subcutaneous, or intravenous route; may be repeated every three to four hours. Pain has been relieved in most patients with not more than three doses daily. Infrequently, selected patients have received single doses as high as 60 mg. *Patients in Labor.* A single, intramuscular 30 mg. dose has been most commonly administered. An intravenous 20 mg. dose has given adequate pain relief to some patients in labor when contractions become regular, and this dose may be given two or three times at two- to three-hour intervals, as needed.

*Children Under 12 Years of Age.* Since clinical experience in children under twelve years of age is limited, the use of Talwin (brand of pentazocine) in this age group is not recommended.

*Duration of Therapy.* Patients with chronic pain who received Talwin for prolonged periods (e.g., over 300 days) experienced no withdrawal symptoms even when administration was stopped abruptly; furthermore, there was no tolerance to the analgesic effect.

*CAUTION.* Talwin should not be mixed in the same syringe with soluble barbiturates because precipitation will occur.

*Treatment of Overdosage or Respiratory Depression.* Talwin has not produced apnea or severe respiratory embarrassment in adults, even in large doses. Occasionally, however, moderate respiratory depression may occur. Means of maintaining proper oxygenation should be available in case of overdosage or respiratory depression, and methylphenidate (Ritalin®) should be administered parenterally. The usual narcotic-antagonists, such as nalorphine, are not effective respiratory stimulants for depression due to Talwin.

How Supplied: *Ampuls of 1 ml.,* containing Talwin® (pentazocine) as lactate equivalent to 30 mg. base and 2.8 mg. sodium chloride, in Water for Injection. Boxes *of* 10, 25, and 100.

*Multiple dose vials of 10 ml.,* each 1 ml. containing Talwin (pentazocine) as lactate equivalent to 30 mg. base, 2 mg. acetone sodium bisulfite, 1.5 mg. sodium chloride, and 1 mg. methylparaben as preservative, in Water for Injection. Boxes *of* 1.

The pH of Talwin solutions is adjusted between 4 and 5 with lactic acid and sodium hydroxide.

**Winthrop**

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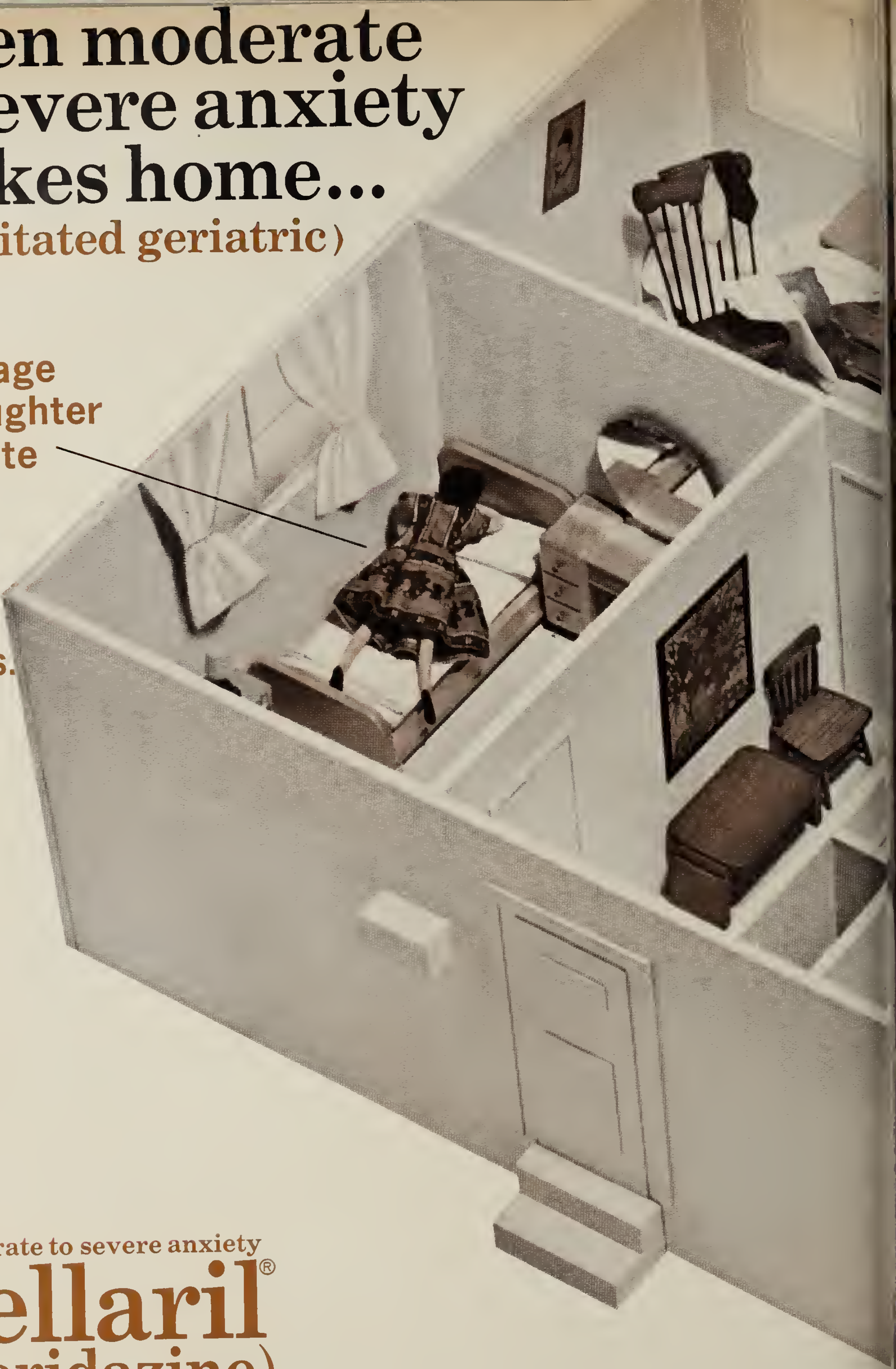
(1150M)

# When moderate to severe anxiety strikes home...

(the agitated geriatric)



His teen-age granddaughter won't invite friends home because of his outbursts.

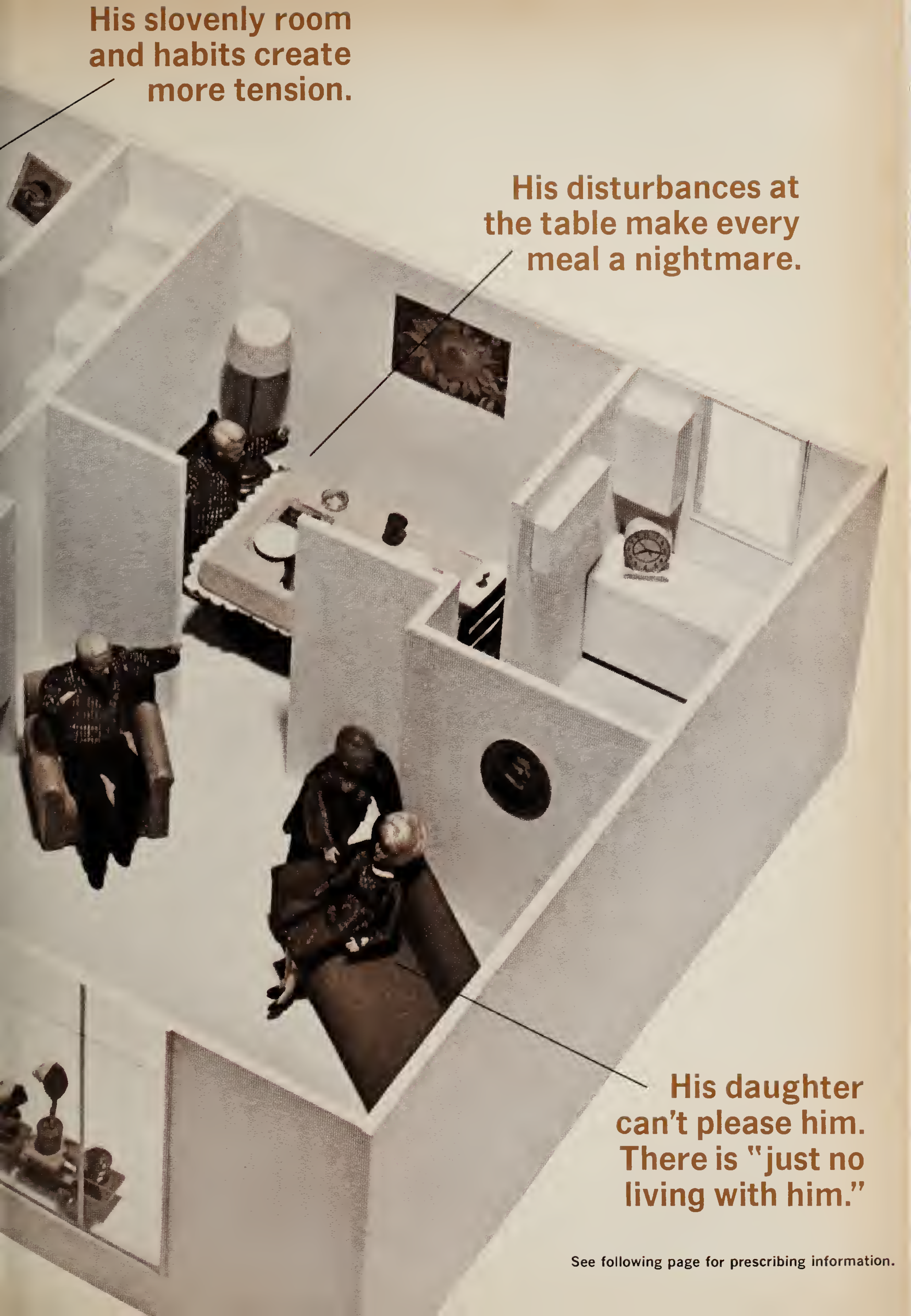
for moderate to severe anxiety

**Mellaril®**

**(thioridazine)**

**25 mg. t.i.d.**

SANDOZ


His slovenly room and habits create more tension.
His disturbances at the table make every meal a nightmare.
His daughter can't please him. There is "just no living with him."

See following page for prescribing information.

## When moderate to severe anxiety strikes home...

Anxiety that *seriously interferes* with the individual's performance at work, at home, or in the community may be regarded as *moderate* to severe in degree.

Mellaril often recommends itself to the treatment of moderate to severe anxiety because it

- helps control the most frequent symptoms: marked tension, agitation, apprehension, restlessness, hypermotility
- often alleviates anxiety-induced somatic complaints
- frequently helps strengthen emotional resources
- helps the patient maintain realistic contact with environment, closer harmony with family

Thus, when you consider the anxiety moderate to severe... consider Mellaril.

**Contraindications:** Severely depressed or comatose states from any cause, and in association with or following MAO inhibitors; severe hypertensive or hypotensive heart disease.

**Precautions:** Hypersensitivity reactions (e.g., leukopenia, agranulocytosis) and convulsive seizures are infrequent. Pigmentary retinopathy has been observed where doses in excess of those recommended were used for long periods of time. May potentiate central nervous system depressants, atropine, and phosphorus insecticides. Where complete mental alertness is required, administer the drug cautiously and increase dosage gradually. In addition, orthostatic hypotension (especially in female patients) has been observed. Epinephrine should be avoided in treatment of drug-induced hypotension.

**Side Effects:** Pseudoparkinsonism and other extrapyramidal disorders are infrequent; drowsiness, especially in high doses early in treatment, may occur; nocturnal confusion, dryness of the mouth, nasal stuffiness, headache, peripheral edema, lactation, galactorrhea, and inhibition of ejaculation are noted on occasion; photosensitivity and other allergic skin reactions may occur but are extremely rare.

*Before prescribing, see package insert for full product information.*

for moderate to severe anxiety

**Mellaril®**
**(thioridazine)**
**25 mg. t.i.d.**

SANDOZ

# mudrane®

*for*

- EMPHYSEMA
- ASTHMA
- CHRONIC BRONCHITIS
- BRONCHIECTASIS

*The fast-disintegrating uncoated tablet gives relief in 15 minutes*

*Each tablet contains:*

| | |
|---|---|
| Potassium Iodide | 195 mg. |
| Aminophylline | 130 mg. |
| Phenobarbital, Caution: May be habit forming | 21 mg. |
| Ephedrine HCl | 16 mg. |

FEDERAL LAW PROHIBITS DISPENSING WITHOUT PRESCRIPTION

Precautions: Usual for aminophylline-ephedrine-phenobarbital. Iodides may cause nausea, long use may cause goiter. Discontinue if symptoms of iodism develop.

Iodide contraindications: tuberculosis, pregnancy.

DOSAGE

One tablet, with full glass of water, 3 or 4 times daily.

*Dispensed in bottles of 100 and 1000 tablets.*

MUDRANE GG—Formula, dosage and package identical to Mudrane—*except*—100 mg. glyceryl guaiacolate replaces the potassium iodide. The value of Mudrane cannot be enjoyed by a small group in which K.I. is contraindicated. Mudrane GG is prepared for this group.

MUDRANE GG ELIXIR—Four 5 cc teaspoonfuls is equivalent to one Mudrane GG tablet. Dosage adjusted to age and weight of child. Mudrane GG Elixir is for pediatric patients and those who think they cannot swallow tablets. Dispensed in pint and half gallon bottles.

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## Meetings

**The American Academy of Pediatrics** will convene for its **36th Annual Meeting** at the Washington Hilton Hotel in Washington, October 21–26, 1967. The registration is expected to total approximately 4,500, including members, families and guests. There will be symposiums on manpower and graduate training, advances in obstetrics of interest to pediatricians, and vaccine progress and problems, also papers on the recognition and management of cardiac failure in infancy, care of burns at home, and the child with chronic renal (kidney) disease.

During Saturday and Sunday, October 21 and 22, scientific programs will be presented by the Sections on Allergy, Anesthesiology, Cardiology, Child Development, Diseases of the Chest, and Surgery and the Committee on Urology. The Section on Military Pediatrics will meet on Tuesday, October 24.

The meeting will feature 11 seminars and 24 round tables for discussion of newborn and premature, pediatric cardiology, infectious diseases, early psychological problems in pediatric practice, and mental retardation.

The Academy meeting is open to physicians who are not pediatricians. Registration fee is $18.00 for Academy members, nonmembers out of school less than 5 years, and physicians in the Armed Forces. Registration fee for nonmember physicians out of school more than 5 years is $50.00.

Interested physicians may write to the American Academy of Pediatrics, 1801 Hinman Avenue, Evanston, Ill. 60204, for a preliminary program and registration forms.

Dr. Robert G. Frazier, Secretary of AAP, is succeeding Dr. E H. Christopherson as Executive Director, the appointment to become effective during the Annual Meeting. Dr. James B. Gillespie has been named Treasurer of the Academy. This position was also previously held by Dr. Christopherson. On September 1 Dr. Christopherson will become Chief of the Bureau of Maternal and Child Health, Department of Public Health, State of California, in Berkeley.

**The 27th Annual AMA Congress on Occupational Health** will be held in Atlanta, Georgia, September 25–26, 1967. There is no registration fee for those who wish to attend the Congress.

Dr. R. Lomax Wells, Chairman of the AMA Council on Occupational Health, will preside at the opening session, Monday morning, September 25. Dr. Milford O. Rouse, President of the American Medical Association, will give the opening address. Following the address Dr. Wells will moderate a panel discussion on Small Plant Problems. He will also preside at the Awards Ceremony at noon. Dr. Gordon S. Siegel, of Silver Spring, an Associate member of the D. C. Medical Society, will present a paper, September 25, on "Occupational Health Programs for Government Employees."

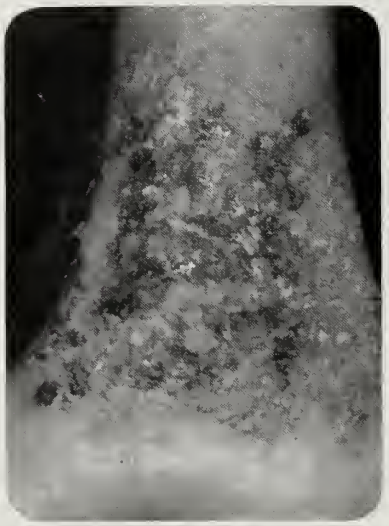
## General News

**Surgeon General William H. Stewart of the Public Health Service** announced, June 7, that travelers arriving in the United States from Mexico will no longer require a certificate of vaccination against smallpox provided they have visited no country other than the U.S. and Mexico during the 14 days prior to their arrival in the States. The last reported outbreak of smallpox in Mexico occurred in 1951. The United States has been free of laboratory-confirmed cases of the disease since 1949.

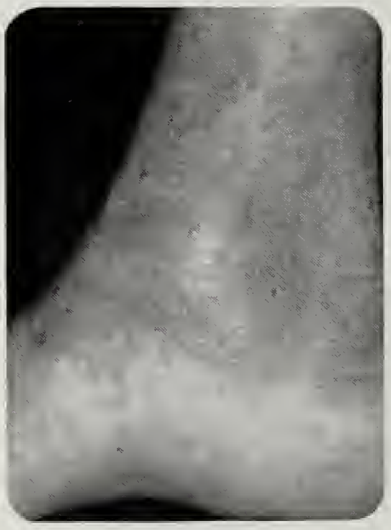
On June 22 the Foreign Quarantine Program moved to the National Communicable Disease Center in Atlanta, Ga. Under the reorganization of the Public Health Service, effective January 1, 1967, the Foreign Quarantine Division became a program of the National Communicable Disease Center, Bureau of Disease Prevention and Environmental Control. Dr. Arthur S. Osborne, Medical Director, is Chief of the Program, and Dr. John H. Hughes, Scientist Director, is Deputy Chief.

**Practitioner-Trainee Fellowships** in radiotherapy, cancer chemotherapy, nuclear medicine, and surgical oncology are being offered as part of the Clinical Cancer Training Program inaugurated by Georgetown University Medical Center and supported by a grant from the National Cancer Institute. A stipend of $1,500 is available for an individual Fellowship depending upon the applicant's qualifications. Fellowships are available for 1-month periods only. Qualified and interested individuals should contact either of the Co-directors of the Program, Dr. J. Robert Andrews and Dr. Bruce I. Shnider.

# Eczema of many years... controlled in two weeks



*Before treatment*



*After treatment*—
with ARISTOCORT Topical
Ointment 0.1% for two weeks

ARISTOCORT® Triamcinolone Acetonide Topicals have proved exceptionally effective in the control of various forms of eczema: allergic, atopic, nummular, psoriatic, and mycotic.

In most cases responsive to topical ARISTOCORT, the 0.1% concentration is sufficiently potent. The 0.5% concentration provides enhanced topical activity for patients requiring additional potency for proper relief.

*Administration and Dosage:* Apply sparingly to the affected area 3 or 4 times daily. Some cases of psoriasis may be more effectively treated if the 0.1% Cream or Ointment is applied under an occlusive dressing.

*Contraindications:* Tuberculosis of the skin, herpes simplex, chicken pox and vaccinia.

*Precautions and Side Effects:* Do not use in the eyes or in the ear (if drum is perforated). A few individuals react unfavorably under certain conditions. If side effects are encountered, the drug should be discontinued and appropriate measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive nonpermeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyodermas will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

Available in 5 Gm. and 15 Gm. tubes and ½ lb. jars.

PHOTOGRAPHS COURTESY OF M. M. NIERMAN, M.D.

**Aristocort®** Topical Ointment 0.1% and Cream 0.1%, 0.5%
Triamcinolone Acetonide
Also available in foam form.

Lederle LEDERLE LABORATORIES, A Division of American Cyanamid Company, Pearl River, New York

406-6

At the Annual Meeting in June of the **Board of Trustees of Medical Service of D. C.** Dr. C. Willard Camalier, Jr. was reëlected President. Dr. F. Preston Titus, of Alexandria, Va., was elected Second Vice President, succeeding Dr. John S. Haught.

Other officers reëlected for 1-year terms were as follows: Dr. Leonard T. Peterson, First Vice President; Mr. George B. McGovern, Executive Vice President of Medical Service, Secretary; and Mr. Douglas R. Smith, President of the National Savings and Trust Company, Treasurer. Two new members were elected to the Board of Trustees, namely, Dr. Kenneth Cruze, representing the Montgomery County Medical Society, and Dr. John J. Walsh, representing the U. S. Public Health Service. Dr. Cruze will serve for 3 years and Dr. Walsh for 2.

Among those reëlected to the Board of Trustees for 3-year terms were Drs. Jack Kleh, Philip H. Philbin, and W. Leonard Weyl.

As a feature of Sight-Saving Month, the **Prevention of Blindness Society of Metropolitan Washington** is planning to offer **free vision tests** to all area 4- and 5-year-olds on Sunday and Monday, October 1 and 2, at the D. C. Medical Society Building. Appointments may be made by telephoning 298-8769.

Two Sections of the D. C. Medical Society have reported new officers. For the **Section on Ophthalmology** they are:

Dr. Melvin G. Alper, *Chairman;* Dr. H. William Gray, *Vice Chairman;* Dr. John W. McTigue, *Secretary-Treasurer;* Drs. L. Edward Perraut and William B. Glew, *members of Executive Committee.*

New officers for the **Section on Internal Medicine and Allied Subspecialties** are:

Dr. John J. Hughes, *Chairman;* Dr. Charles W. Humphries, Jr., *Vice Chairman;* Dr. Lewis H. Biben, *Secretary;* and Dr. Stephen N. Jones, *Treasurer.*

**The D. C. Society of Internal Medicine** has elected the following officers for 1967–68:

Dr. Jack Kleh, *President-elect*; Dr. Lewis H. Biben, *Secretary*; and Dr. Stephen N. Jones, *Treasurer.*

Dr. George A. Kelser has taken office as President.

**Georgetown University** has added 7 new members to its Board of Regents, the University's lay advisory board, who will serve 3-year terms beginning July 1. One of them is Dr. Hugh H. Hussey, Director of the Division of Scientific Activities of the American Medical Association since 1963. He served as Dean of Georgetown University School of Medicine from 1958 to 1962.

## Attention—Metropolitan Washington Physicians

Please complete and return the survey questionnaire on "Continuing Education" sent you by the Metropolitan Washington Regional Medical Program. Your Medical Society is the grantee for this program.

Many physicians have delayed completion of this questionnaire because of difficulty in completing items 4 and 5. The Coördinator suggests that you simply state the approximate number of national meetings and formal conferences attended or participated in, if you do not remember the details. If you have lost the form, call 223-6490 and ask for another form. Do it now. The information you supply will be helpful in planning programs in continuing education for the Region.

In the first issue of its new publication, *Heart News*, the **Washington Heart Association** reported that the Chairman of its Research Committee, Dr. Alvin E. Parrish, had announced grants for the fiscal year 1967–68 totaling more than $80,000, to benefit 19 specific projects. Eight of the grants will be conducted under the direction of members of the D. C. Medical Society. Their names and the titles of their projects are:

Dr. R. A. Massumi, George Washington University Medical Division, D. C. General Hospital: (1) "Combined Radioactive Lung Scanning and Pulmonary Angiography in Differential Diagnosis between Pulmonary Embolus and Parenchymal Lung Disease," and (2) "Critical Evaluation of the ECG Syndrome of Right Bundle-branch Block—Left Axis Deviation: Its Relationship to Heart Block and Bradycardia-dependent Bundle-branch Block."

Dr. James R. Snyder, Doctors Hospital: "Correlation of the Blood Levels of Digitalis with Its Physiological Response in Normal Subjects."

Dr. Basedo Balkissoon, Howard University College of Medicine: "Cardiodynamics of Endotoxin Shock."

Dr. Frank A. Finnerty, Jr., Georgetown University Medical Division, D. C. General Hospital: "Lack of Importance of Plasma Volume Reduction in the Early Fall of Arterial Pressure during Drug-induced Saluresis."

Dr. Norman C. Kramer, George Washington University School of Medicine: "Effect of Altered Blood Viscosity on Renal Function."

Dr. James E. McClenathan, Children's Hospital: "Evaluation of the Effects of Ganglionic Blocking Agents on the Acid-base Balance in Newborn Perfusions."

Drs. Marion Mann and Andrew F. Burton, Howard University College of Medicine: "Electron Microscope and Histochemical Evaluation of Myocardial Biopsies in Primary Myocardial Disease."

**Two former staff members of the American Medical Association** have accepted new appointments. **Dr. Charles C. Edwards,** formerly Director of the Division of Socio-Economic Activities, is Vice President of Booz, Allen & Hamilton, international management consultants, with headquarters in Chicago. **Dr. Walter S. Wiggins,** who was Secretary of the AMA Council on Medical Education for 8 years, is President of the Chicago Medical School.

**Dr. A. Rex Kirkley,** of Dallas, Texas, has been **appointed Assistant Manager of the Washington Office** of the AMA, effective July 1. A graduate of the University of Texas Medical Branch at Galveston, he has been Medical Director of Blue Cross-Blue Shield of Texas since 1963.

## Personals

**Dr. James G. Sites** has been appointed Professor and Chairman of the Department of Obstetrics and Gynecology at George Washington University School of Medicine, succeeding Dr. Robert H. Barter. Dr. Sites has been associated with George Washington University since he received his medical degree there in 1947. He served as intern and resident at the University Hospital, and joined the medical faculty in 1955 as an instructor. He is attending physician at D. C. General Hospital and consultant in obstetrics and gynecology to the National Institutes of Health, the National Naval Medical Center, and Walter Reed Army Medical Center.

**Dr. Sanford L. Billet** has resigned his position as Chief of the Alcoholic Rehabilitation Clinic at 14th and Q Streets, N.W., which position he had held since 1960. He was honored by his staff members at a luncheon and gift presentation on May 31. He will devote full time to his private practice of psychiatry.

## Correspondence

CLEVELAND, OHIO, June 1, 1967

TO PRESIDENT ECKER:

As you know, the AMA Volunteer Physicians for Vietnam program is financed by the United States Agency for International Development (USAID) and administered, under contract, by the American Medical Association. Physicians sent to South Vietnam under the program serve a 60-day tour of duty at one of 18 provincial civilian hospitals. The volunteer receives only his transportation and an expense allowance of $10.00 a day; otherwise his services are entirely unpaid.

During the first 2 years of operation, 294 physicians have departed to serve voluntarily in Vietnam; this number includes 25 physicians scheduled to depart this month. These volunteers, who come from 46 states, the District of Columbia and the Canal Zone, have over the past 2 years voluntarily provided over 45 man-years of medical care to the civilian population of South Vietnam.

Before my retirement as President of the AMA, I wish to thank you as President of your State Medical Association for your past support of this program. During the first year of operation under the AMA, 175 physicians have served in Vietnam, an increase of 47 per cent in the number of volunteers over the first year of operation. We can anticipate a comparable increase in requirements during the coming year. For this reason I am writing to urge continuing support of this program in your state and by your . . . specialty organizations. We need more applications, particularly from internists, general practitioners, general surgeons, and orthopedic surgeons.

CHARLES L. HUDSON, M.D.
*President, American Medical Association*

ALEXANDRIA, VA., June 2, 1967

THOMAS M. PEERY, M.D.
CHIEF OF SERVICE IN PATHOLOGY
GEORGE WASHINGTON UNIVERSITY HOSPITAL
WASHINGTON, D. C.

DEAR DR. PEERY:

I certainly was glad to see your editorial in the MEDICAL ANNALS OF THE DISTRICT OF COLUMBIA, May 1967, page 304. The points that you made in regard to laboratory charges are essentially the same as the ones that I made in an article in *Medical Economics* last year. Unfortunately, many pathologists thought that the article was attacking them instead of attacking the system.

There are several general principles of medical care that I think we can all agree upon, and the sooner that we can work together to further these principles the better off everyone will be.

1. Patients should be provided the best possible care at the least possible cost. Anytime a more econom-

ical method of carrying out a procedure can be devised the savings should be passed on to the patient.

2. Every patient should be charged for what he gets so that no procedure is subsidizing another procedure. Because it is easy to itemize laboratory tests, extra charges here have been used to pay for physicians' services in other categories.

3. No physician should be in the position where he can make a profit from ordering a specific laboratory procedure. The physician who is in charge of carrying out the procedure should of course receive ample compensation for investment in equipment and supervision; and the physician who is collecting the specimens should receive compensation commensurate with the service rendered. The present system permits many internists to do their history and physicals for nothing if they order enough laboratory tests. This makes laboratory procedures appear to be a much larger portion of the total medical bill than it really is.

4. A pathologist should be properly compensated by the hospital for other services that are rendered. The fees that you derive from the performance of laboratory tests should not be used to pay the cost of autopsies that are done for the benefit of the hospital. If your charges are correct for private patients, it should not be necessary for you to cut them 50 per cent in order to subsidize special research projects that are paid for by other groups.

If we discuss these problems openly and work together toward these common goals, we will improve the overall quality of medical practice by eliminating many of the abuses that are inherent in the present system.

Sincerely yours,
James M. Moss, M.D.

# Obituaries

## Robert Joseph Bosworth, A.B., M.D.

(1898–1967)

Dr. Robert J. Bosworth, a general practitioner in Washington since 1928, died, June 9, 1967, at his home, 4636 34th Street North, Arlington, Va. A native of Washington, D. C., Dr. Bosworth was born, May 3, 1898, to Henry H. and Emma C. Bosworth. He graduated from McKinley High School, and he received both his undergraduate degree (1921) and his medical degree (1925) from George Washington University. He interned at George Washington University Hospital and served a 2-year residency at the same hospital.

During his many years of practice in the District of Columbia, and until he retired in 1963, he maintained his offices at 811 Eighth Street, N.E. He taught physiology at George Washington University from 1926 to 1931. He was on the attending staff of Sibley Memorial Hospital during his entire practice, having served as President of the Medical Council, Chief of the Medical Staff, and Chairman of the Medical Staff's Executive Committee. In 1959 he was named Sibley's "Doctor of the Year." He had also served on the staffs of Providence and Children's Hospitals, and on the staffs of Emergency and Garfield Memorial Hospitals before they merged into the Washington Hospital Center.

Dr. Bosworth was an Active member of the Medical Society of the District of Columbia since 1931. He was a member of the American Medical Association, the Southern Medical Association, the American Academy of General Practice, and the George Washington University Medical Alumni Association.

He leaves his wife, Mrs. Florence Thompson Bosworth; a son, Robert J. Bosworth, Jr., of Philadelphia; 2 brothers, Herbert H. and Howard Bosworth, both of Arlington; also 3 sisters, Mrs. Edith Ford, of Arlington, Mrs. Helen McDonnell, of Washington, and Mrs. Emma Martin, of Watertown, N. Y.

## Luis Francisco Thomen, M.D., M.S., M.P.H., D.P.H.

(1912–1967)

Dr. Luis F. Thomen, medical liaison officer of the World Health Organization, died suddenly at the Graduate Hospital of the University of Pennsylvania in Philadelphia, July 10, 1967. He was an Honorary member of the Medical Society of the District of Columbia.

Dr. Thomen was born in Santiago de los Caballeros, Dominican Republic, October 10, 1912. He received his medical degree from the University of Santo Domingo in 1936. The same year he came to the United States for postgraduate work at Columbia University and at Tulane University. He practiced his profession in his own country until 1941, when he returned to the United States for advanced studies in the School of Hygiene and Public Health at Johns Hopkins.

Dr. Thomen served in the Dominican Republic as Secretary of State for Health and Public Assistance from 1944 to 1947. From 1947 to 1953, and again from 1959 to 1960, he was Ambassador from the Dominican Republic to the United States. In 1950, while residing in Washington, he was elected to Honorary membership in the D. C. Medical Society.

He became associated with the World Health Organization in 1946 as head of the Dominican delegation to the International Health Conference of the United Nations. He joined the World Health Organization in New York in 1962.

He was a member of many scientific organizations, including the Dominican Medical Association, the American Society of Tropical Medicine, American Association for the Advancement of Science, the Society of American Bacteriologists, and the American Public Health Association. His contributions to the literature were numerous. He had been decorated by his own government and by Peru and the Argentine Republic. In 1948 he was awarded the Gold Cross of Honor of the Military Surgeons of the United States.

## Joseph Hyram Roe, A.B., M.A., Ph.D.

(1892–1967)

Dr. Joseph H. Roe, Emeritus Professor of Biochemistry of George Washington University School of Medicine, died, May 18, 1967, at his home, 2939 Van Ness Street, N.W. He was beloved by the medical community as both a teacher and scholar. As a researcher he developed many biochemical diagnostic methods which are in common clinical usage today.

Born in Winchester, Va., December 27, 1892, Dr. Roe received his A.B. degree from Roanoke College, M.A. from Princeton University, a doctorate in chemistry from George Washington University in 1923, and a doctorate in physiological chemistry from Yale University in 1934.

He joined the staff of the George Washington University as Assistant Professor of Biochemistry in 1919. Appointed Professor in 1922, he served as Chairman of the Department from 1922 to 1932 and from 1938 to 1959, when he retired.

During World War II he was scientific consultant to the War Department on the selection of medical trainees, consultant to the National Research Council's Committee on Food Composition, and Gas Officer for the Washington Region of the Office of Civilian Defense.

Author of "The Principles of Chemistry" and "A Laboratory Guide in Chemistry," he was also co-author of "A Laboratory Manual of Biochemistry" and had written numerous articles for scientific journals.

Among his professional affiliations were the American Association for the Advancement of Science, American Society of Biological Chemistry, American Chemical Society, American Institute of Nutrition, American Association of Clinical Chemists, Society for Experimental Biology and Medicine, American Medical Association (Affiliate), and the Washington Academy of Medicine. He was an Associate member of the D. C. Medical Society from 1930 to 1934 and a member of the Cosmos Club.

He leaves his wife, Mrs. Clara Grace Lauck Roe, of the home address, and a son, Dr. Joseph Hyram Roe, Jr., of Washington.

### Atrial Pulsation of Chest Wall—Stapleton and Lindberg

(*Continued from page 520*)

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## Indications

### Hypertension

**Such as hypertension with or without congestive failure, where Hygroton can be used alone or in conjunction with other agents**
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### Edema

**Such as edema associated with: congestive heart failure or renal disease**
(*Precaution:* Because of the possibility of progression of renal damage, periodic determination of the BUN is indicated. Discontinue if the BUN rises.)
**or hepatic cirrhosis**
(Hypoproteinemia, if present, must be corrected concomitantly.
*Precaution:* Take special care: discontinue if liver dysfunction is aggravated, since hepatic coma may be precipitated.)
**or steroid administration**
**or obesity**
**or the premenstrual syndrome**
**or pregnancy, including toxemia**
(*Warning:* Use with caution in pregnant patients, since the drug may cross the placental barrier and adverse reactions which may occur in the adult, e.g. thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc., are potential problems in the newborn.)

## Contraindications

**Severe Renal or Hepatic Disease and Demonstrated Hypersensitivity**

## Other general warnings, precautions and adverse reactions

*Warning:* With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue enteric-coated potassium supplements immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur.

*Precautions:* Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Hygroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria.

Take special care in severe ischemic heart disease and in patients receivin corticosteroids, ACTH, or digitalis. Salt restriction is not recommended.

*Adverse reactions:* Nausea, gastric irritation, vomiting, anorexia, constipation and cramping, dizziness, weakness, restlessness, hyperglycemia, hyperuricemia, headache, muscle cramps, orthostatic hypotension, aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, dysuria, impotence, transient myopia, skin rashes, urticaria, purpura, necrotizin angiitis, acute gout, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonge administration. Other reactions reported with this class of compound include: jaundice, xanthopsia, paresthesia, and photosensitization.

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# BOOK REVIEWS

**Postoperative Complications in Neurosurgical Practice: Recognition, Prevention, and Management.** NORMAN H. HORWITZ, A.B., M.D., AND HUGO V. RIZZOLI, A.B., M.D. Price, $17.50. Pp. 427, illustrated. Baltimore: Williams & Wilkins, 1967.

This achievement represents the first specific dedication to the countless complications one may encounter in the complete range of neurosurgical practice. There is a natural tendency to avoid the publicizing of complications of surgery and poor results. Therefore, this comprehensive volume is both timely and proper, and the authors are to be congratulated for their undertaking. It represents much more than the title designates. There is an abundance of valuable information pertinent to the treatment of neurosurgical conditions and when applied will improve results and reduce morbidity. Interesting historical references abound and are particularly plentiful in the chapter on Intracranial Neoplasms. The bibliography of every section is extensive and embraces the important world literature of the English, German, French, Spanish and Italian languages. This feature alone should make it a valuable reference book.

The authors have divided their work into 5 parts. The first part is devoted to Intracranial Surgery, and it is appropriate that this demanding and vexatious segment of neurosurgery should require about half of the text. All types of intracranial tumors have been discussed with pertinent comments about the methods of handling them and about the alternate methods with their incumbent risks and complications. Aneurysms and arteriovenous malformations provoke wide diversity of management, and these perilous lesions have been dealt with in detail. There is less extensive commitment to head injuries, intracranial infections, and various intracranial operations for relief of pain, but a clear summary of complicating factors is available. The remaining 4 parts apply to Cranio-spinal, Spinal and Peripheral Nerve Surgery and to Diagnostic Contrast Studies. The chapters on Herniated Discs and Spinal Cord Injury are well illustrated with relevant roentgenograms and photographs. The section on Diagnostic Contrast Studies contains a detailed review of the various complications connected with angiography and a discussion related to techniques and types of contrast material available.

The broad review of world literature has produced a collection of various important reports of complications and, in addition, the authors have inserted personal experiences and exemplary case reports from hospital affiliates. Thus, this volume of data on complications and the sound judgment that may be exercised to avoid some of these disagreeable occurrences makes it an important treatise for the library of all who are concerned with the daily demands of clinical practice of neurosurgery. It is precise and well written. Hopefully, the authors will undertake revision of their work from time to time as the rapid advances of neurological surgery demand it.

STACY L. ROLLINS, M.D.

**Renal Neoplasia.** Edited by J. STANTON KING, JR., M.D. with 52 participants. Price, $18.50. Pp. 688, with 246 illustrations. Boston: Little, 1967.

This volume contains the transactions, which include the original papers and discussions, of the International Conference on Renal Neoplasia which was held in Brasilia, Brazil, September 10–12, 1965. The contents include contributions by world authorities in the different fields of basic science and clinical investigation and various types of therapy, including chemotherapy. It also involves cytochemical procedures and molecular biological contributions.

WILLIAM P. HERBST, M.D.

**Neonatal Respiratory Adaptation.** Proceedings of Interdisciplinary Conference on Neonatal Respiratory Adaptation, December 6–9, 1963, Princeton, N. J. Sponsored by the National Institute of Child Health and Human Development, Public Health Service, National Institutes of Health, U. S. Department of Health, Education, and Welfare. THOMAS K. OLIVER, JR., M.D., Scientific Editor, AND WANDA M. BURNETT, Technical Editor. Price (paper), $1.25. Pp. 251, illustrated. Washington, D. C. 20402: Superintendent of Documents, U. S. Government Printing Office, 1966 (PHS Publ. No. 1432).

The Proceedings of this Interdisciplinary Conference on Neonatal Respiratory Adaptation, held in December 1963, represent an instance in which the outstanding workers in a rapidly advancing field were brought together under NIH sponsorship for in-depth interchange. The result is a state-of-the-art document on research in perinatal respiration and circulation. One of the unfortunate results of the complexity of editing such proceedings is that 4 years have intervened between the Conference and the book's publication. Nevertheless, since we are privileged to look into current work and even future plans of the participants at the time of the Conference, the material presented is still fresh and germane by 1967 standards.

The title belies the scope of the book, which begins with consideration of the implanting ovum. Indeed, one is nearly halfway through the book before the fetus emerges from the uterus. Yet so important are intrauterine events and the sweep of embryonic development to understanding the sudden adjustments which the newborn must make to loss of the placenta and air breathing, that this approach seems the only thorough and scholarly one. Much primary data are presented, with abundant tables, graphs, and photomicrographs. Occasionally one is bothered by the conference style,

*(Continued on page 43)*

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## Book Reviews

(*Continued from page 41*)

with participants interrupting one another for 1-line comments, militating against orderly presentation of the subject. But on the whole the style is lively and readable.

This book will be of greatest interest to the researcher in the field of neonatal physiology, as well as to those with major interest in the care of newborns. The diagnosis and therapy of disease are not dealt with at all, but valuable insight is given into the variations from normal physiology occurring in hyaline membrane disease. The slant is entirely toward basic physiology, and readers without some background in dye dilution curves, pressure gradients, and measurements of pulmonary function may find the going difficult. Yet this book is full of valuable information and the price is right—well worth it for those who make the effort to read and understand.

Gordon B. Avery, M.D.

**Hearts. Their Long Follow-up.** Paul Dudley White, M.D., and Helen Donovan. Price, $12.00. Pp. 357, with 63 illustrations. Philadelphia: Saunders, 1967.

This is not a textbook but a delightful and highly readable narration of the case histories of cardiac patients whom Dr. White has followed, many for decades. Two themes are apparent throughout this book: (1) Heart disease is not always a crippling and rapidly fatal disease, but in many it is compatible with normal longevity, and (2) careful and long-term follow-up of patients by an interested physician can contribute greatly to the knowledge and experience of the physician and much to the natural history of diseases.

The 86 items, making up a total of 20 chapters, are systematically arranged, beginning with follow-up histories of patients with normal and borderline findings, followed by that of patients with heart disease of various etiological classifications or with major disease manifestations. Short comments at the beginning or end of chapters or often following illustrative case histories provide neatly packed capsules of information related to natural history of disease, medical progress in diagnosis and treatment, interesting events in the lives of the patients, and most important of all, bits of wisdom and philosophy from the Dean of the Cardiologists of our time. This is not just a publication of successes. Dr. White has pointed out with great honesty and modesty errors in diagnosis and professional judgment made in certain cases, including the particular lesson learned from the mistake. Examples of this are seen in reported cases with constrictive pericarditis (pp. 207–208). Again, on page 289, after optimistically concluding that the arrhythmias of the Wolff-Parkinson-White syndrome are of an innocuous nature, he carefully points out that one of his patients died suddenly during an attack. On page 144 he relates an instance where a 71-year-old man with a long follow-up study of angina was considered to have coronary disease but autopsy revealed noncoronary myocardial disease. Such reported observations have helped in the recognition of this type of myocardial disease in the aged.

The material in this book reflects the great enthusiasm, general optimism, and the genuine interest in people and medicine so typical of the senior author. The collection of this patient data is not just a secretary's summary of the notes taken from routine office records and visits. I have witnessed the collection of some of this patient information, as our mutual interest in more recent years has found Dr. White and me traveling in the same parts of the world. Former patients, residing in a city where he is participating in a medical meeting or other function, on hearing of his presence are likely to phone or call at his hotel. This to most physicians might be a simple exchange of greeting or an unwelcome event, but not with Dr. White. The patient would eventually give an interval history and receive a current examination. His "little black book," which he is never without, soon had another neatly written set of notes for the secretary member of the team to transfer to the office record on his return.

Helen Donovan, his secretary and co-author, was not the only help he received in this travelogue through the life history of heart disease. Help came from another Donovan, Agnes (Mrs. Bernard Walsh of Washington), who was an earlier secretary, and also, through his inspired interest, from a large number of assistants, cardiac fellows and residents, graduate and undergraduate students at Massachusetts General Hospital, beginning before the year 1920. Many of these have become renowned cardiologists in different parts of the world. Their greatest delight is to send bits of follow-up information on patients previously seen by Dr. White. A note of acknowledgment as well as this long list of physicians is included in the preface of the book. I consider it an honor to be included in that list and to have provided him with frequent follow-ups on one of his prominent patients.

This book should be of interest to practicing bedside clinicians and hopefully to medical students being initiated into clinical medicine. This type of book will soon disappear and be replaced by the recording dictaphone and an impersonal computer compilation of data, in keeping with the present era. Perhaps the future book itself will be written by the computer.

Thomas W. Mattingly, M.D.

**Ciba Foundation Symposium: Ethics in Medical Progress with Special Reference to Transplantation.** Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Maeve O'Connor, B.A. Price, $11.75. Pp. 257. Boston: Little, 1966.

This monograph reports the proceedings of a Symposium on Ethics in Medical Progress, with special

(*Continued on page 44*)

## Book Reviews

(*Continued from page 43*)

reference to transplantation, held March 9–11, 1966, in London, England. This conference, under the distinguished chairmanship of Lord Kilbrandon, touched with poignancy the problems relating to the ethics involved in tissue transplantation specifically and, peripherally, to the problems of the volunteer in medical research. Both of these subjects are timely and important to anyone engaged in medical investigation and to many prominent jurists involved in determining the value of human life. The presentations in the initial section of the text present a historic development and a chronology of what has been done thus far in defining the ethics of such transplantation procedures as blood transfusions, corneal transplantation, and, more recently, solid organ transplantations, such as that of the kidney and liver. The participants in this Symposium consisted of both distinguished physicians and surgeons engaged in transplantation and distinguished jurists who spoke on the legal, moral, and ethical aspects of permission for transplantation; on conditions under which donors were acceptable; and on the point of defining death for postmortem organ transplantation. In addition to these discussions the volume has 6 appendices which contain the Nuremberg Code, the Declaration of Helsinki, the British Human Tissue Act of 1961, and the District of Columbia Tissue Bank Act of 1962. They provide the reader with essential background material and models of legal documents dealing with tissue banks and tissue donations.

This conference and the proceedings will have a profound effect on all individuals involved in human experimentation of any type, including drug research, and are in keeping with the changing concepts of human rights to which all of us give service.

The conference came to no final conclusions except in relation to the use of prisoner volunteer donors for tissue transplantation. Their use is not ethical because these individuals do have a great deal of restraint of freedom under the best of circumstances. On this basis, Dr. Starzl has discontinued the use of prisoner volunteers in his transplant program.

The questions and problems raised at this conference should prove of great value in the future for drafting laws and developing concepts for the greatest protection of the individual without the stifling of much needed research activity. Many of the statements made during the course of this conference are especially apropos in the light of changing regulations by the Food and Drug Administration and the U. S. Public Health Service in regard to the necessity for a full, knowledgeable consent by all participants in human research. I would recommend the reading of this monograph to all individuals engaged in medical investigation involving humans and to all other individuals who have concern for human welfare.

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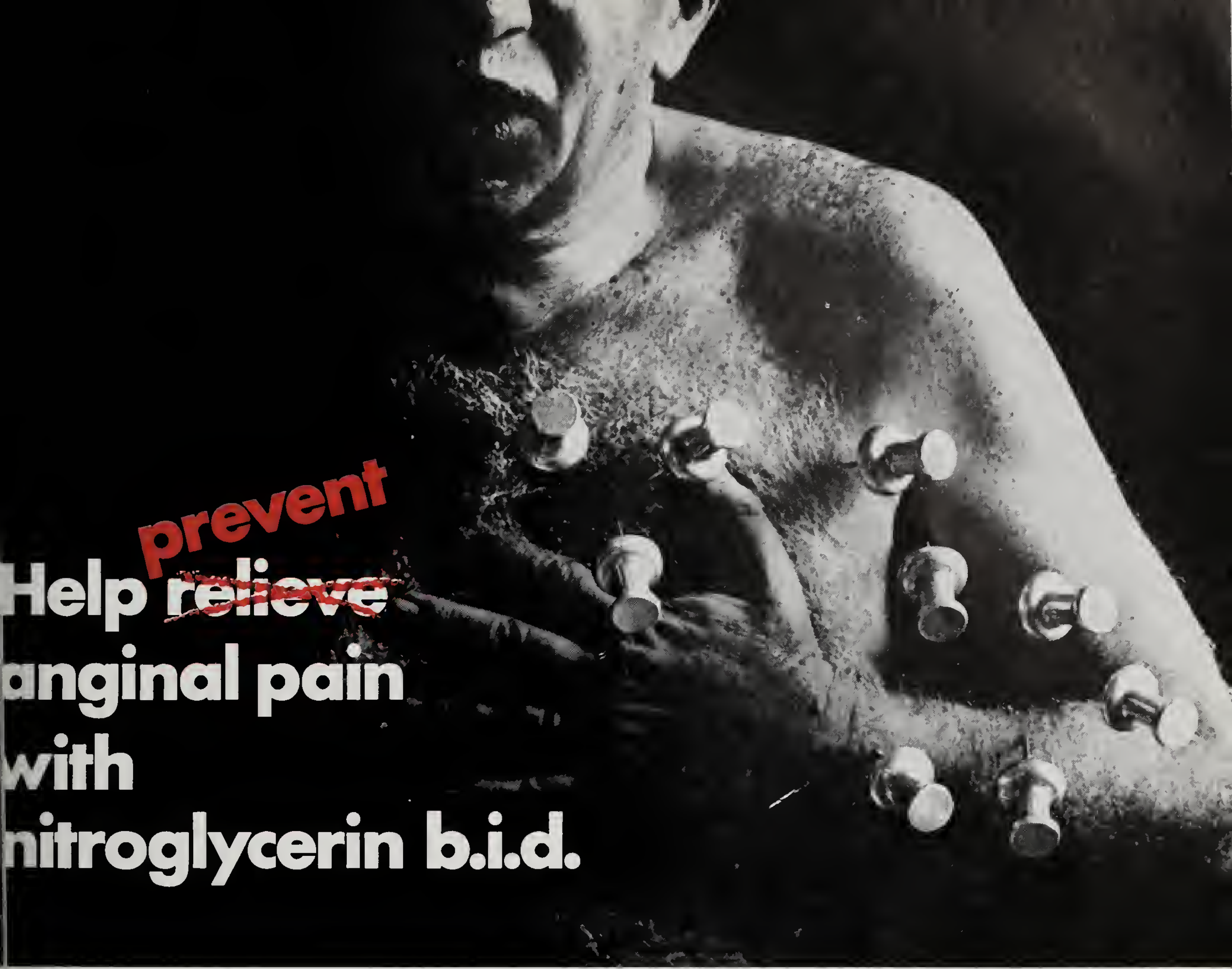

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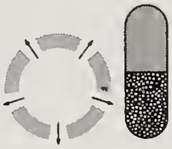

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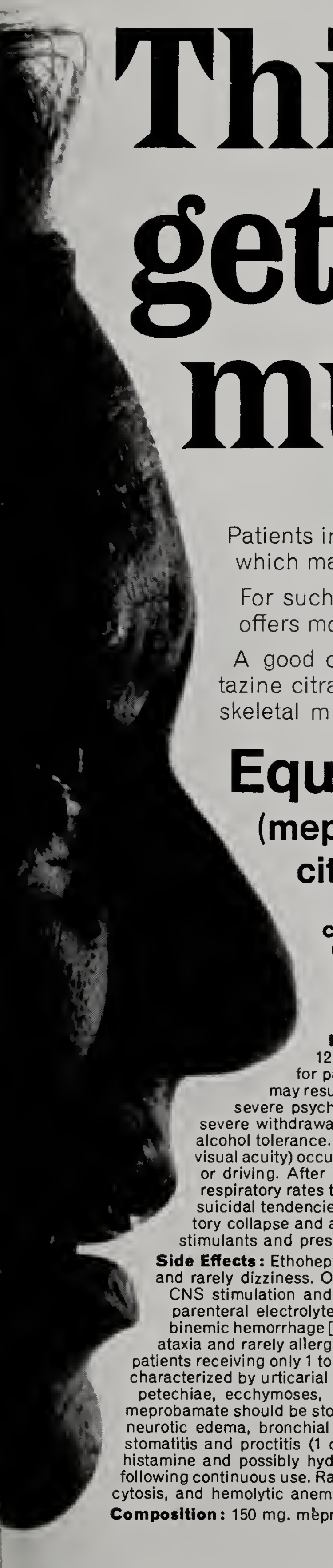

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**Side Effects:** Ethoheptazine and aspirin may occasionally cause nausea, vomiting, epigastric distress, and rarely dizziness. Overdosage may result in CNS depression (drowsiness and lightheadedness) or CNS stimulation and salicylate intoxication (requires induced vomiting or gastric lavage, specific parenteral electrolyte therapy for ketoacidosis and dehydration, and observation for hypoprothrombinemic hemorrhage [usually requires whole blood transfusions]). Meprobamate may cause drowsiness, ataxia and rarely allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically such as with epinephrine, antihistamine and possibly hydrocortisone. A few cases of leucopenia, usually transient, have been reported following continuous use. Rarely, cases of aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported; almost always, in the presence of known toxic agents.

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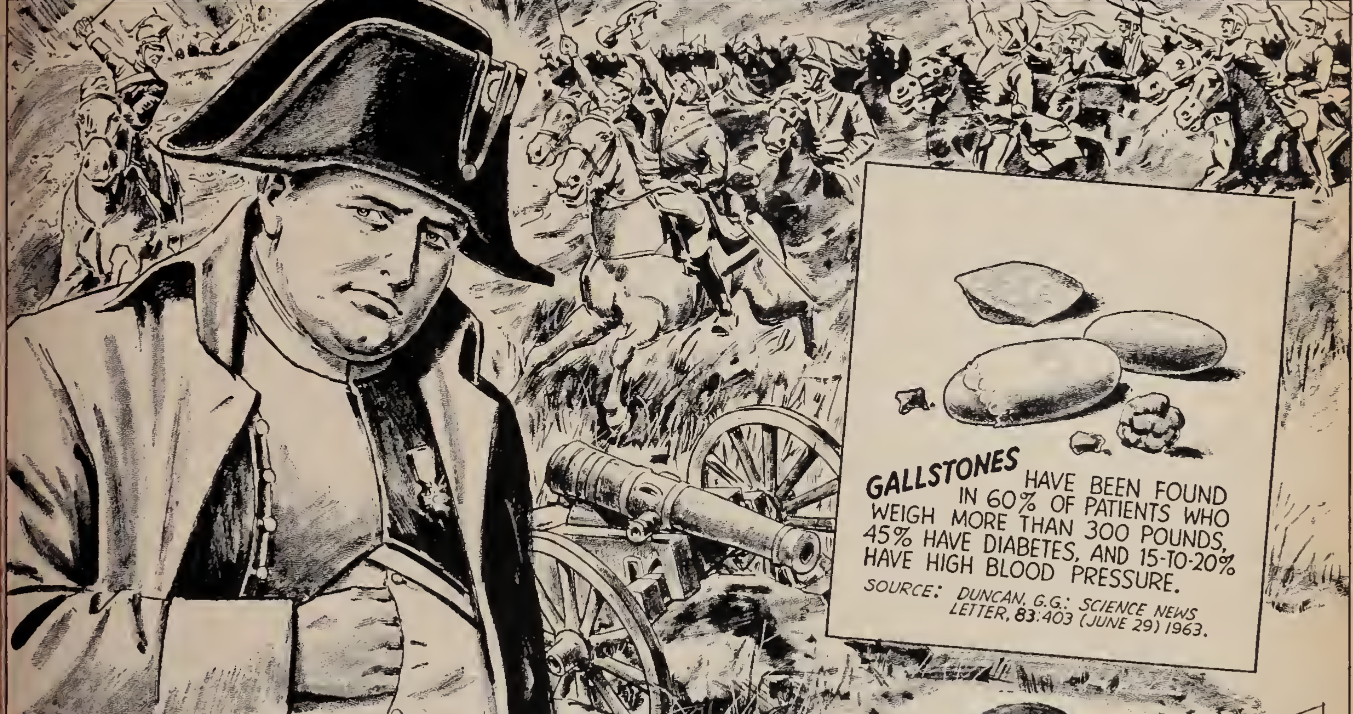

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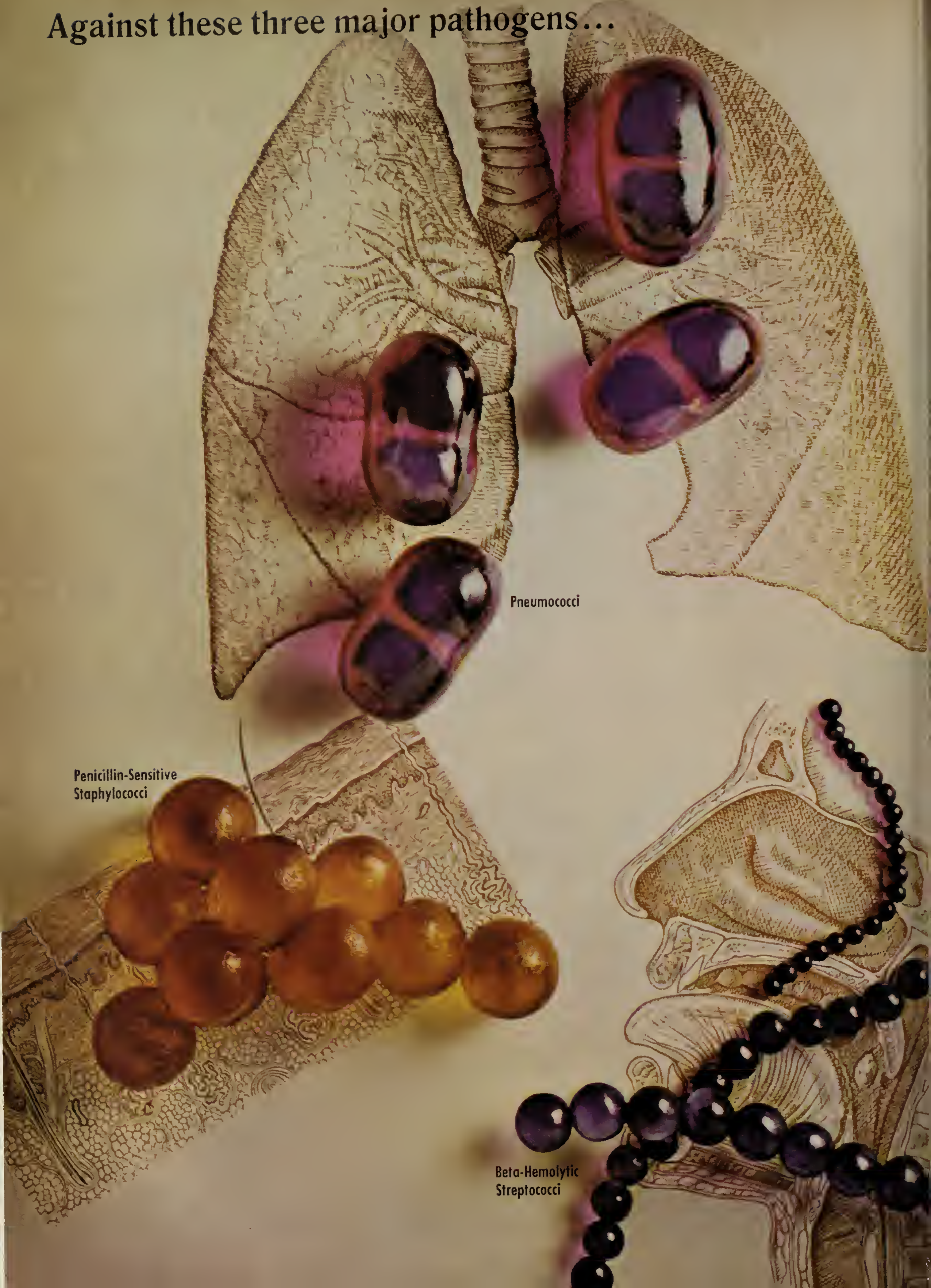
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| Methicillin | 1.6 | 0.4-6.3 | 0.2 | 0.1-0.4 | 0.2 | 0.1-1.6 |
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Adapted from Klein, J. O., and Finland, M.: New England J. Med.,269:1019, 1963.

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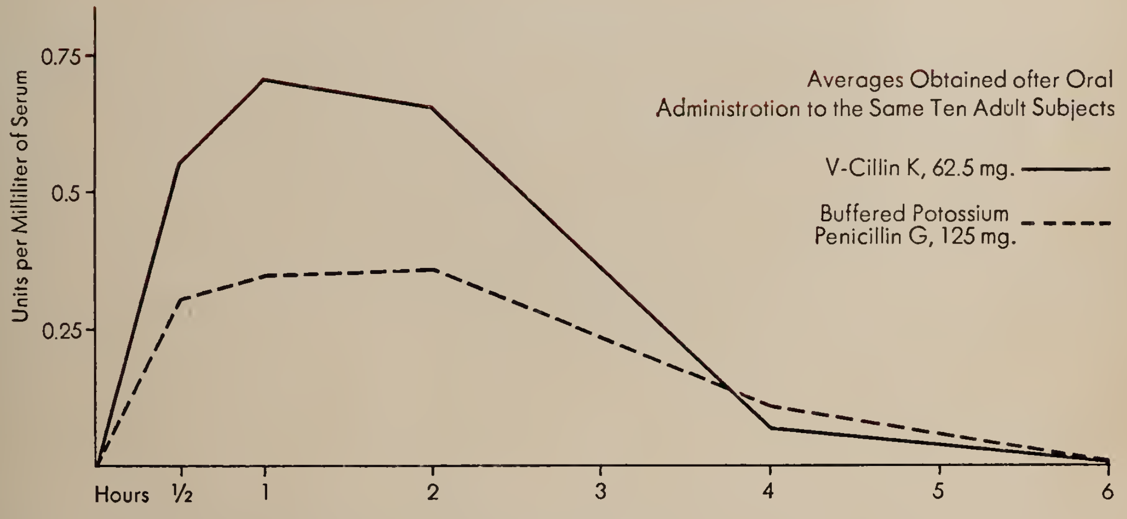

Adapted from Griffith, R. S., and Black, H. R.: Current Ther. Res., 6:253, 1964.

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**Contraindication:** V-Cillin K should not be administered to a patient with a history of penicillin hypersensitivity.

**Warnings:** In rare instances, the use of penicillin may cause acute anaphylaxis which may prove fatal unless promptly controlled. This type of reaction appears more frequently in patients with a history of sensitivity reactions to penicillin and in those with bronchial asthma or other allergies. Resuscitative drugs should be readily available for emergency administration. These include epinephrine and pressor drugs (as well as oxygen for inhalation) for relief of immediate allergic manifestations and antihistamines and corticosteroids for delayed effects.

**Precautions:** V-Cillin K should be used cautiously, if at all, in a patient with a strongly positive history of allergy.

In prolonged therapy with penicillin, and particularly with hi parenteral dosage schedules, frequent evaluation of the renal o hematopoietic systems is recommended.

In suspected staphylococcus infections, proper laboratory studi (including sensitivity tests) should be performed.

The use of penicillin may be associated with the overgrowth pencillin-insensitive organisms. In such cases, its administration shou be discontinued, and appropriate measures should be taken.

**Adverse Reactions:** Although serious allergic reactions are much le common with administration of oral penicillin than with intramuscul forms, manifestations of penicillin allergy may occur.

Penicillin is a substance of low toxicity, but it does possess a sign cant index of sensitization. The following hypersensitivity reactic associated with the use of penicillin have been reported: skin rash ranging from maculopapular eruptions to exfoliative dermatitis; u caria; and reactions resembling serum sickness, including chills, fev edema, arthralgia, and prostration. Severe and often fatal anaphylo has occurred (see Warnings). Hemolytic anemia, leukopenia, thro bocytopenia, and nephropathy are rarely observed side-effects o are usually associated with high parenteral dosage.

**Administration and Dosage:** For Tablets V-Cillin K and for V-Cillin Pediatric, the usual dosage ranges from 125 mg. (200,000 units) thr times a day to 500 mg. (800,000 units) every four hours. For infan the daily dosage may be 50 mg. per Kg. of body weight divided ir three doses.

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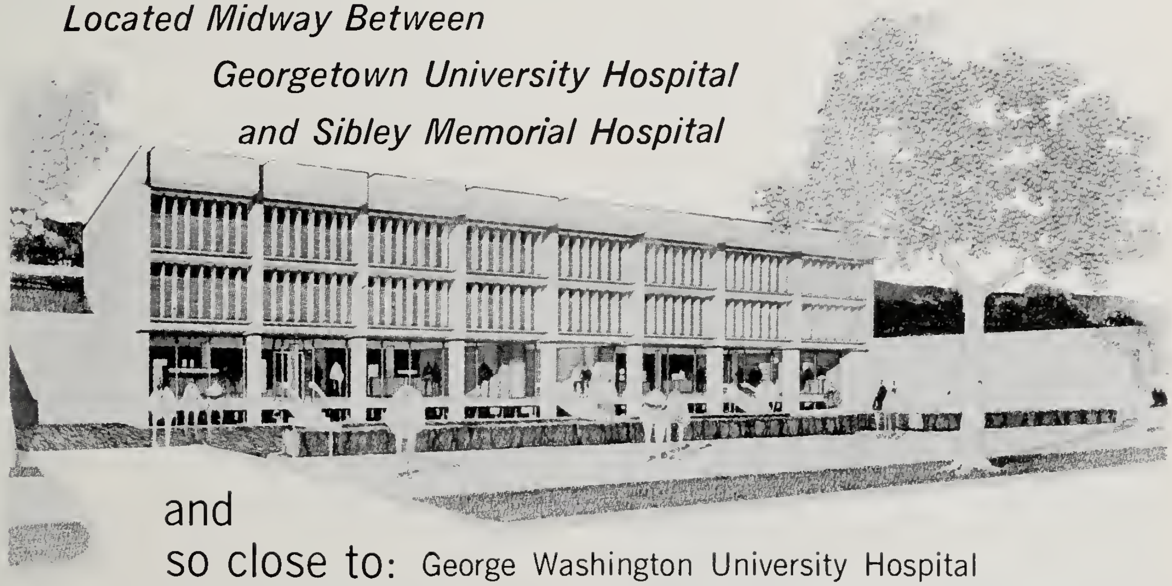

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**Precautions:** Limit dosage to smallest effective amount in elderly or debilitated patients (not more than 1 mg, one or two times daily initially) to preclude ataxia or oversedation, increasing gradually as needed or tolerated. As is true of all CNS-acting drugs, until correct maintenance dosage is established, advise patients against possibly hazardous procedures requiring complete mental alertness or physical coordination. Driving during therapy not recommended. In general, concurrent use with other psychotropic agents is not recommended. If such combination therapy is used, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium (diazepam), such as phenothiazines, barbiturates, MAO inhibitors and other antidepressants. Advise patients against simultaneous ingestion of alcohol or other CNS depressants. Safe use in pregnancy not established. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Observe usual precautions in impaired renal or hepatic function. Periodic blood counts and liver function tests advisable in long-term use. Cease therapy gradually.

**Side Effects:** Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances, acute hyperexcited states, hallucinations); changes in EEG patterns during and after drug treatment. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms (convulsions, tremor, abdominal and muscle cramps, vomiting, sweating) similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.

**Dosage**—*Adults:* Mild to moderate psychoneurotic reactions, 2 to 5 mg b.i.d. or t.i.d.; severe psychoneurotic reactions, 5 to 10 mg t.i.d. or q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; muscle spasm with cerebral palsy or athetosis, 2 to 10 mg t.i.d. or q.i.d. *Geriatric patients:* 1 or 2 mg/day initially, increase gradually as needed and tolerated. (See Precautions)

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*Adverse Reactions:* The most common are nausea, edema and drug rash. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ul-

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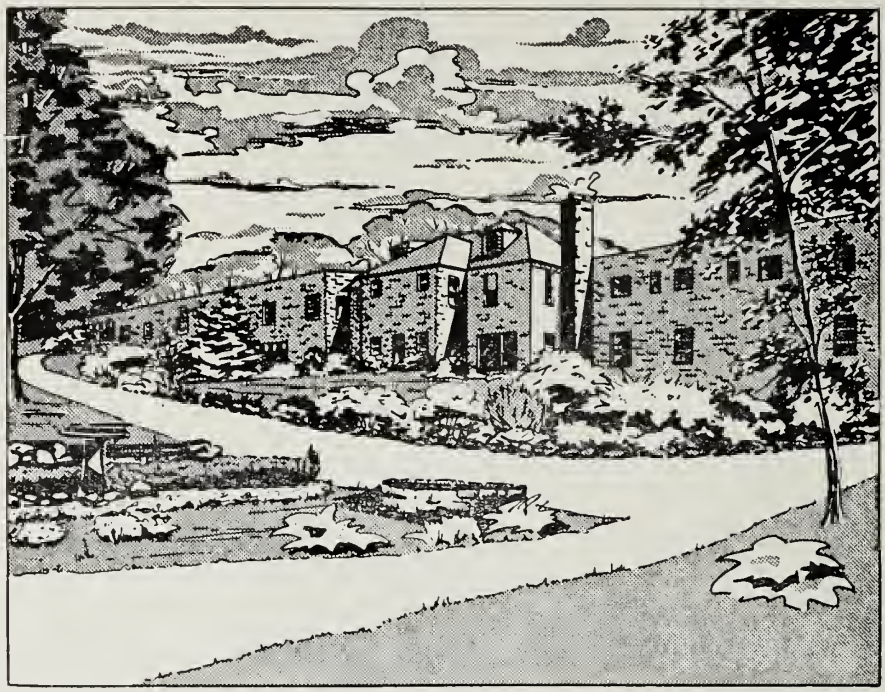

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I. G. Canter, M.D., and P. C. Luchsinger, M.D.

**Treatment of Facial Fractures**
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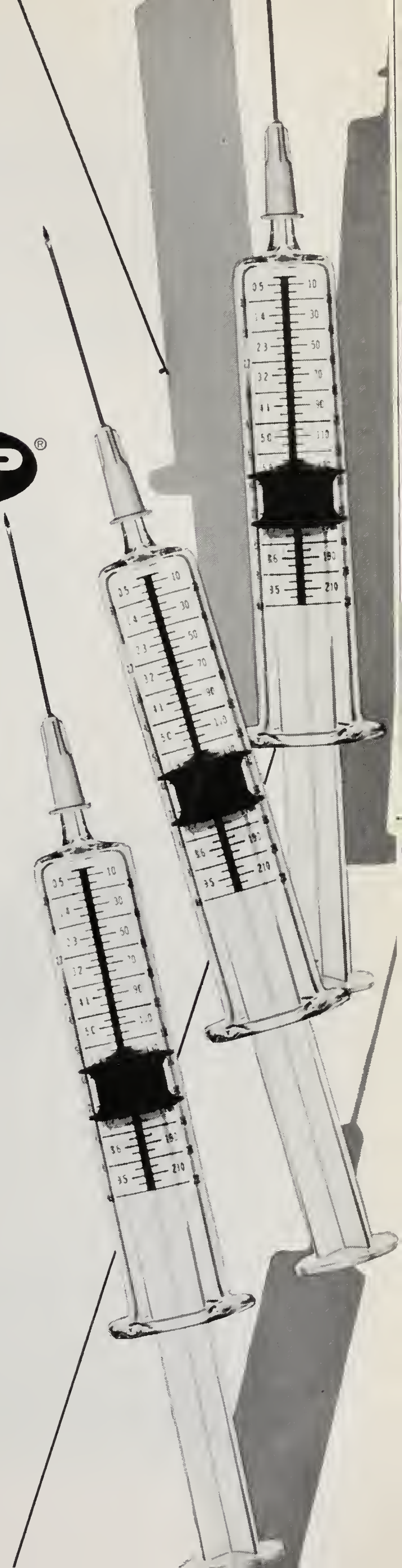

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*Based on Statistical Report, U.S. Dept. Commerce, ed. 86, and Fisher, G. F., and Vavra, H. M.: Pub. Health Rep. 80:961 (Nov.) 1965.

Note: DEXTROSTIX is not meant to replace the more precise analytical laboratory procedures such as needed in glucose tolerance testing.

**AMES COMPANY,** Division Miles Laboratories, Inc., Elkhart, Indiana 46514 428R67

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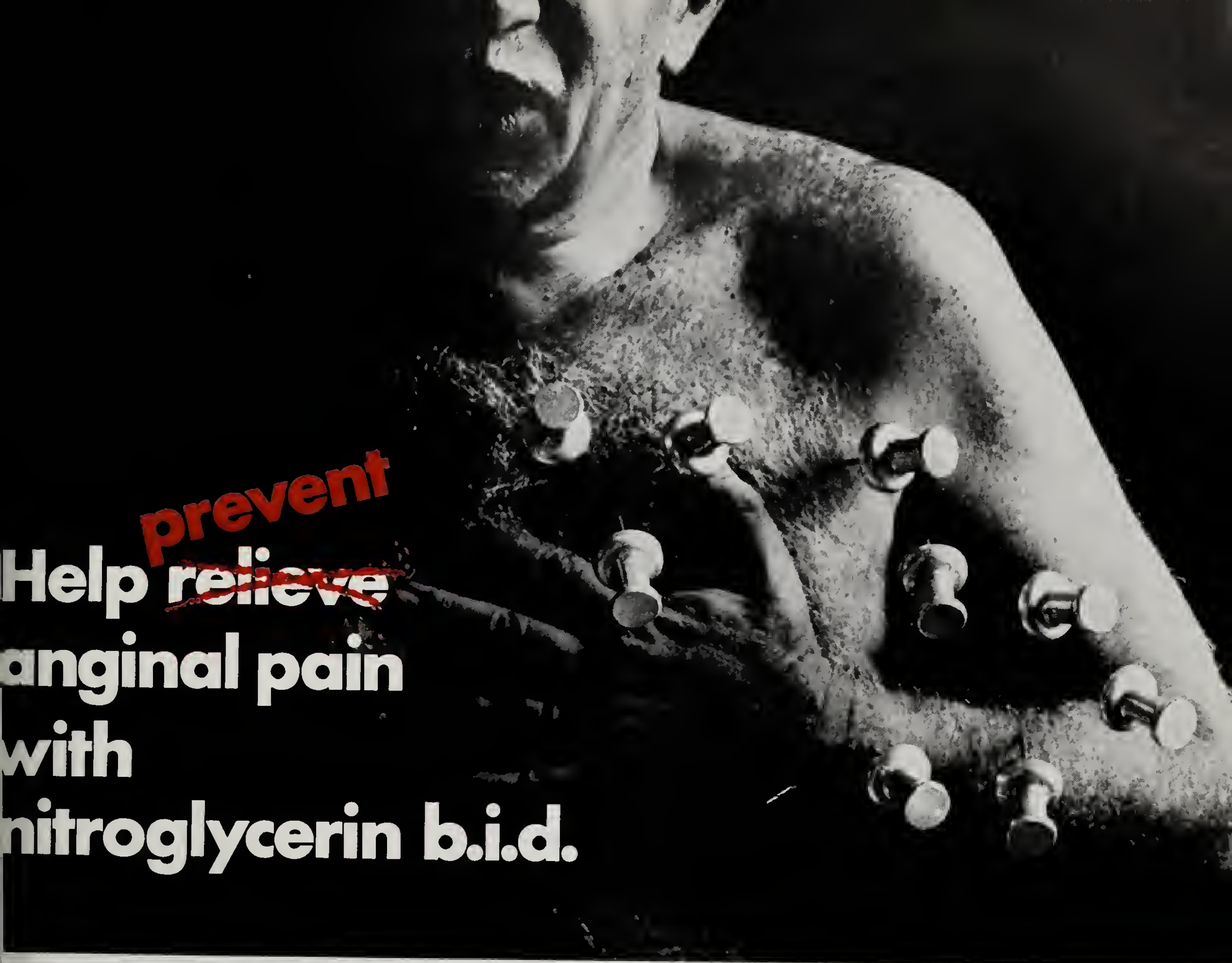
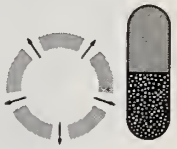


## Unique Nitrospan micro-dialysis process*
## adds an important dimension–TIME–to nitroglycerin therapy

Ielps decrease frequency and severity of attacks; often ncreases exercise tolerance. Decreases need for subingual nitroglycerin, increases patient confidence. mooth, continuous release independent of gastrointesinal functions reduces headache and other side effects hat might result from peak concentrations of tablet or ntermittent-release preparations.

**ndication and Dosage:** For prophylactic use only in anina pectoris, 1 capsule every 12 hours. **Precautions:** For rophylaxis only, not for relief of acute anginal attacks. olerance to nitrites may develop on long-continued use. **ontraindications:** Idiosyncrasy to nitroglycerin, and arly myocardial infarction. **Side Effects:** With use of itrites, transient headache, postural hypotension, nausea and vomiting may occur. Overdoses may cause flushing, dizziness, tachycardia, headache and syncope.

*__The micro-dialysis cell.__ Nitrospan's timed-release mechanism is different from those usually employed in sustained-action capsules, which rely on unpredictable digestive processes. The nitroglycerin in Nitrospan capsules is contained within hundreds of dialysis cells of controlled permeability. The contents of each micro-dialysis cell are released by diffusion rather than disintegration, at a continuous rate independent of gastrointestinal action. Only the presence of fluid is required.



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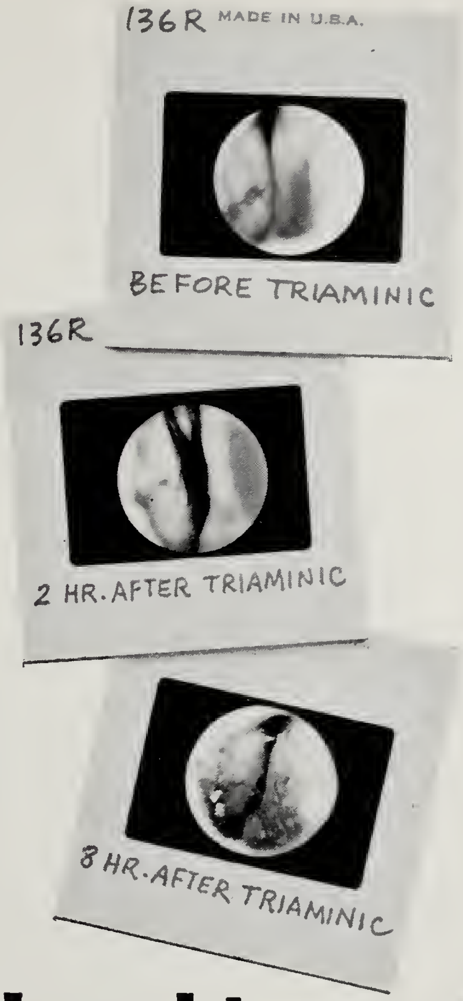

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A study being conducted by the Department of Otolaryngology, Greater Baltimore Medical Center is stockpiling evidence that points to the fast action and prolonged relief effected by Triaminic in the treatment of nasal congestion.

Begun in March 1966, the study to date has encompassed 85 patients with common nasal disorders—and measured their response to recommended doses of Triaminic tablets.

Timed to release its oral nasal decongestant and two antihistamines within 8 hours, Triaminic was found to effect partial or complete relief in better than 82% of the subjects treated. Clearing nasal obstruction. Reducing turbinate swelling. Making breathing easier.

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Each timed-release tablet contains:

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Side effects: Occasional drowsiness, blurred vision, cardiac palpitations, flushing, dizziness, nervousness or gastrointestinal upsets.

Precautions: The patient should be advised not to drive a car or operate dangerous machinery if drowsiness occurs. Use with caution in patients with hypertension, heart disease, diabetes or thyrotoxicosis.

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*Contraindications:* Barbiturates should not be administered to anyone with a history of porphyria, nor should they be given in the presence of uncontrolled pain, because excitement may result.

*Warning:* May be habit-forming.

*Precautions:* Tuinal should be used cautiously in patients with decreased liver function, since prolongation of effect may occur.

*Adverse Reactions:* Idiosyncrasy, such as excitement, hangover, or pain, may appear. Hypersensitivity reactions occur in some patients, especially in those with asthma, urticaria, or angioneurotic edema.

*Overdosage:* C.N.S. depression. Symptoms—Depression of respiration and of superficial and deep reflexes, slight constriction of the pupils (in severe poisoning, dilation), decreased urine formation, lowered body temperature, coma. Treatment—Symptomatic and supportive (gastric lavage; intravenous fluids; maintenance of blood pressure, body temperature, and adequate respiration). Dialysis may speed removal of barbiturates from body fluids.

*Dosage:* 50-200 mg. (¾-3 grains) at bedtime.

[031767]

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# New view of an oral contraceptive at work

Although suppression of ovulation remains the primary mode of action of oral contraceptives, newer knowledge indicates that products like Norinyl-1—a combination of both low-dosage progestogen and estrogen for the full treatment cycle—may provide multiple action that helps explain their unexcelled record of contraceptive effectiveness. This report explores the possible secondary protective mechanisms offered by combined hormonal administration.

Accumulating evidence has indicated that sparse, highly viscous cervical mucus has a possible adverse effect on the motility and survival of spermatozoa.

The estrogen-opposing progestational ingredient of Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.) changes the usual midcycle picture of a thin, watery cervical mucus. The result—a built-in barrier that appears to inhibit sperm from reaching the ovum should one be released. The inset in the adjoining photograph shows immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

See last page for contraindications, precautions, side effects and dosage.

# How the estrogen-opposing action of Norinyl-1 creates cervical mucus that may be hostile to sperm penetration

Normally, estrogen activity during the fertile midcycle stimulates the production of a profuse and watery cervical mucus that permits maximum sperm motility and promotes penetration.

But what happens when Norinyl-1 is administered? Its potent progestogen, norethindrone, opposes estrogen stimulation of cervical mucus. Consequently, the amount of mucus decreases and its viscosity increases. This results in a sparse but thick mucus barrier that appears to diminish the vitality of the sperm and to impair its powers of penetration.

## The role of viscous cervical mucus as a secondary action of Norinyl-1

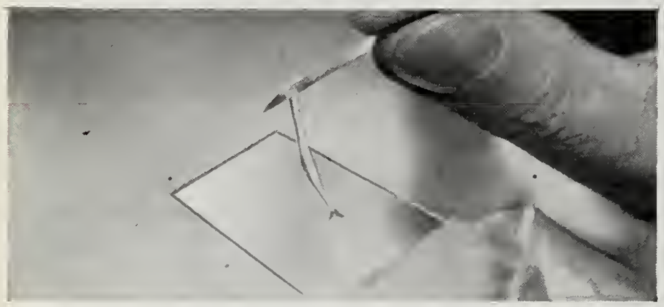
In a report on 89 patients taking this medication,* cervical mucus obtained from cycle day 5 to cycle day 29 appeared scant and thick and exhibited little or no Spinnbarkeit.

In the opinion of this investigator, the effect on cervical mucus may be sufficient to prevent conception.

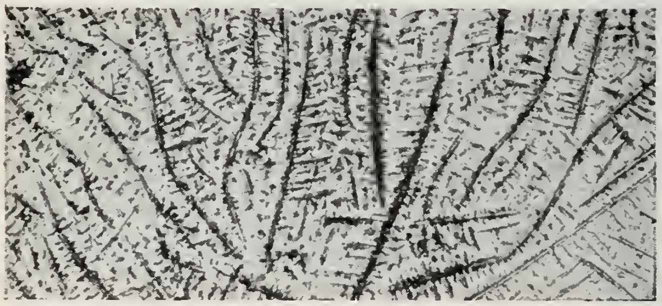
---

*Cohen, M. R.: Symposium: Mechanisms of Action of Low Dosage Oral Contraceptive, Yale University Medical Center, New Haven, Conn., April 6, 1967.

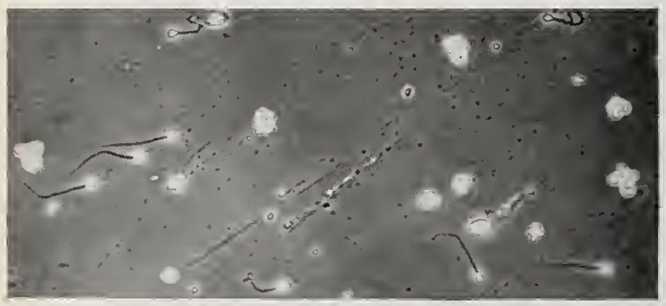
### Normal cervical mucus at midcycle in untreated patient is known to permit sperm motility... promote sperm penetration.



Cervical mucus is thin and watery with a stretchability (Spinnbarkeit) of 15 to 20 cm.

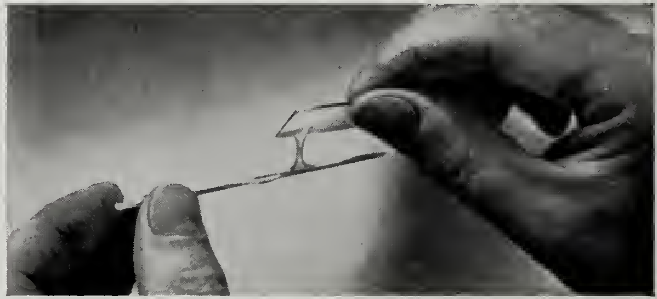


Thin, watery mucus crystallizes into this well-defined, fernlike pattern within a minute.

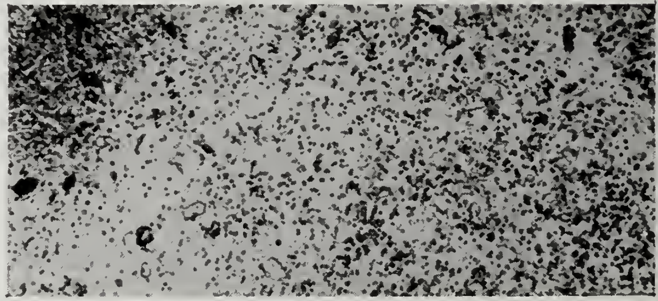


Spermatozoa appear healthy, are active and freemoving.

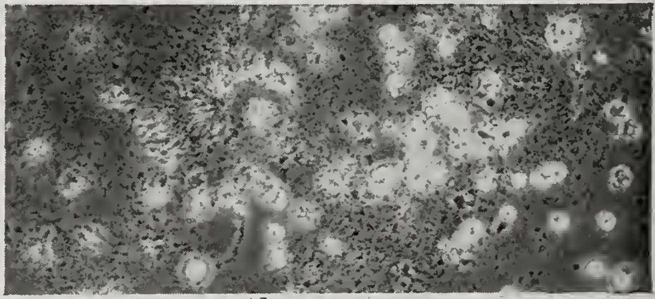
### Viscous cervical mucus at midcycle produced by Norinyl-1 appears to impair sperm vitality... inhibit penetration.



Cervical mucus is scanty, thick and viscous. Spinnbarkeit is 1 cm. or less.



In thick, viscous cervical mucus the fern pattern is poorly defined or absent.

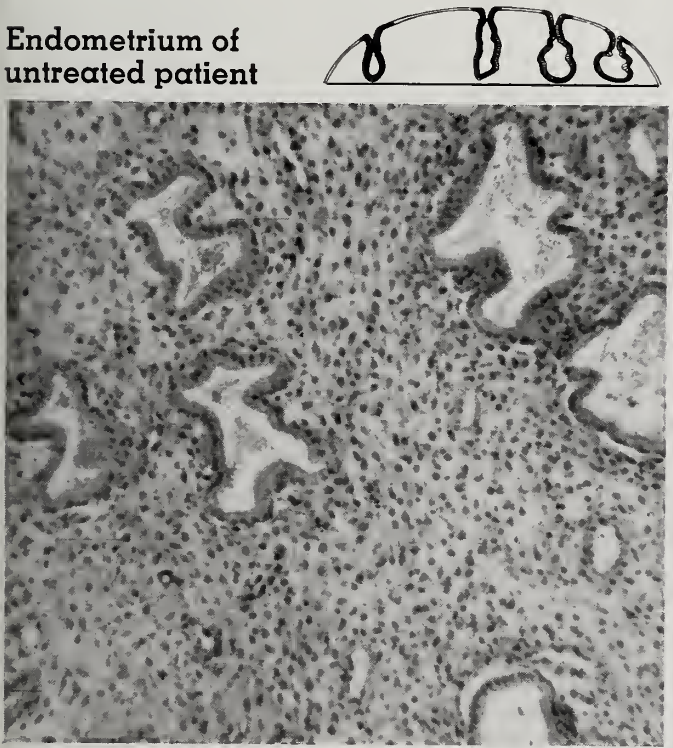


Immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

# How Norinyl-1 alters normal endometrial responses—another possible protective mechanism

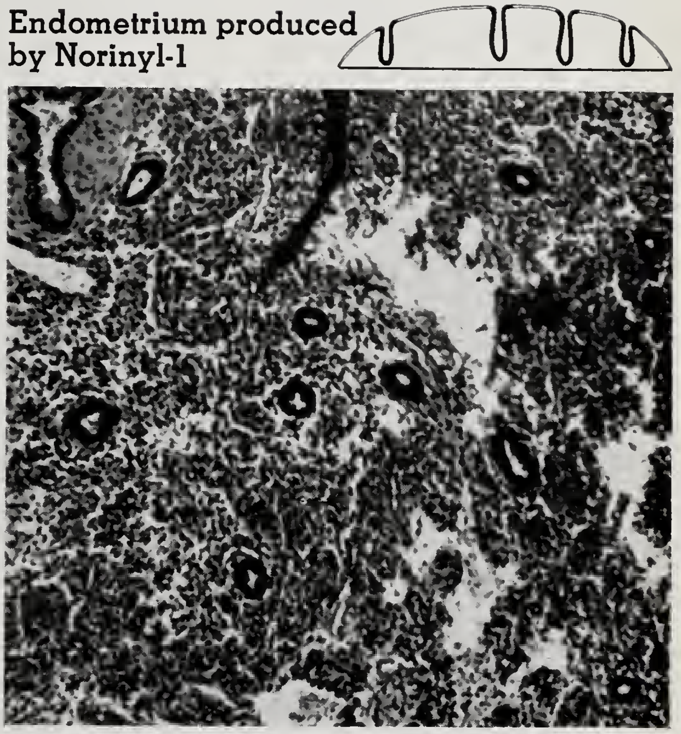
Let us suppose that an ovum is released—as occurs in an occasional, rare case—and somehow a sperm succeeds in penetrating the cervical mucus barrier. Should this come about, one additional action of Norinyl-1 may protect the patient from unwanted pregnancy. The theory is that progestogen intake makes endometrial tissue unreceptive to implantation.

**Endometrium of untreated patient**



Normally, the endometrium progresses through a proliferative phase stimulated by estrogen and a secretory phase stimulated by progesterone. During the secretory phase the endometrium is receptive to the fertilized ovum.

**Endometrium produced by Norinyl-1**



When Norinyl-1 is administered its progestogen component—norethindrone—accelerates the secretory phase and suppresses glandular and vascular development.

new **Norinyl-1**® tablets

(norethindrone 1mg. c̄ mestranol 0.05mg.)

See last page for contraindications, precautions, side effects and dosage.

effective fertility control
on half the previous dosage

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of the established
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Reduction of oral contraceptive dosage to lowest effective levels has become a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now available in a new strength in which *both* norethindrone and mestranol are reduced 50 percent. Studies show that Norinyl-1 achieves fertility control with only 1.05 mg. of combined progestogen and estrogen per tablet.

Norethindrone was first reported for use as a progestational agent in human beings in 1955. Norethindrone 2 mg. with mestranol 0.1 mg., as an oral contraceptive, is currently in use by over 2,000,000 women. Clinical experience now establishes that Norinyl-1 also amply meets the criteria of reliability and safety.*

*Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965.

PRESCRIBING INFORMATION

**Contraindications:** 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

**Warnings:** 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of Norinyl-1 in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

**Precautions:** 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with Norinyl-1. Therefore, if such tests are abnormal in a patient taking Norinyl-1, it is recommended that they be repeated after the drug has been withdrawn for 2 months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibroids may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac, or renal dysfunction, require careful observation. 5. Although a cause and effect relationship has not been established, Norinyl-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, as in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged Norinyl-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Norinyl-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. A cause and effect relationship has not been demonstrated. 11. Because of the effects of estrogens on epiphyseal closure, Norinyl-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask the onset of the climacteric. 13. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

**Side Effects:** The following adverse reactions have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma, breast changes (tenderness, enlargement and secretion), loss of scalp hair, change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, erythema multiforme, erythema nodosum, hemorrhagic eruption, migraine, rash (allergic), itching, rise in blood pressure in susceptible individuals, mental depression.

The following occurrences have been observed in users of oral contraceptives. A cause and effect relationship has not been established: thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory results may be altered by the use of oral contraceptives: increased bromsulphalein retention and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in $T^3$ values), metapyrone test, pregnanediol determination.

Other side effects reported to have occurred in association with use of this drug are dizziness, hirsutism, pains in legs, back, chest and abdomen, dysuria, drowsiness, vaginal discharge, libido increased and decreased, eruptions, hypermenorrhea, hypomenorrhea, increased appetite, G.U. infections, varicose veins, abdominal fullness, acne, headache, nervousness, allergies, blurred vision, pain in eyes, and itching in eyes. *For complete clinical data, see package insert.*

**Dosage and Administration:** 1. One tablet of Norinyl-1 is administered orally for 20 days beginning on day 5 of the menstrual cycle. (Count day 1 of the cycle as the first day of menstrual bleeding.) Repeat this dosage schedule for each cycle. 2. If no menstrual period occurs after a cycle of treatment (20 tablets) in which patient adhered to the schedule, the patient must be instructed to resume taking the Norinyl-1 tablets 7 days after the previous 20-day course was completed. For example, if the last pill of a previous cycle had been taken on a Sunday, then a new cycle of treatment should begin on the following Sunday. 3. In the postpartum woman, it is recommended that the first cycle of treatment should begin on day 5 of the first menstrual cycle. However, Norinyl-1 should not be administered during lactation.

**Availability:** Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.)—Dispensers of 20 and 60 and bottles of 250 tablets.

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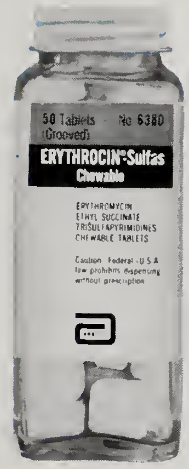
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In clinical trials[1,2], this orange-flavored tablet was given to 55 patients, aged four months to 18 years.

Diagnoses (multiple in some cases) represented a cross section of bacterial infections commonly seen in pediatric office practice.

Therapy was given from three to 12 days, with an average of six days.

Of the 55 patients, 30 were reported cured within 72 hours, while 22 showed partial recovery within the same time, and subsequent clinical cure.

**A clinical cure rate of 94.5%**

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87 patients were treated[1,2]—all children, ages four months to 15 years.

The diagnoses were multiple in some cases and were chiefly bacterial infections of the respiratory tract.

Dosage was maintained from three to 10 days; average treatment was five days. All of the ill children accepted the orange-flavored suspension favorably.

53 were clinically cured within 72 hours, while 32 showed partial relief within the same time, and subsequent clinical cure.

701358

**A clinical cure rate of 97.7%**

ABBOTT

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on next
page

1. Case Reports on File, Dept. Clin. Development, Abbott Laboratories.
2. Polley, R.F.L., Use of Erythromycin-Sulfas in Office Practice, Western Med., 7:177, July, 1966.

**ERYTHROCIN®-SULFAS**
Brief Summary

**Contraindications:** Known sensitivity to erythromycin or sulfonamides. Because of the possibility of kernicterus with sulfonamides, do not use in pregnancy at term, premature or newborn infants.

**Warnings:** As with other forms of sulfonamide therapy, carefully evaluate patients with liver or kidney damage, urinary obstruction, or blood dyscrasia. Deaths have been reported from hypersensitivity reactions and blood dyscrasias following use of sulfonamides. Perform blood counts and liver and kidney function tests if used repeatedly at close intervals or for long periods.

**Precautions, Side Effects:** Occasionally mild abdominal discomfort, nausea or vomiting may occur with erythromycin, generally controlled by reduction of dosage. Mild allergic reactions (such as urticaria and other skin rashes) may occur. Serious allergic reactions have been extremely infrequent. Use sulfonamides with caution in patients with a history of allergy. Assure adequate fluid intake to prevent crystalluria and institute alkali therapy if indicated. If overgrowth of nonsusceptible organisms occurs, withdraw the drug and institute appropriate treatment. If a patient should show signs of hypersensitivity, appropriate countermeasures (e.g. epinephrine, steriods, etc.) should be administered and the drug withdrawn.

**Adverse Reactions:** Sulfonamide therapy may be associated with headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.

Side effects due to erythromycin are infrequent, but occasional abdominal discomfort, nausea, or vomiting, urticaria and other skin rashes may occur.

**Supplied:** The Granules for Oral Suspension come in bottles of 60 ml. and 150 ml. The Chewable tablets are in bottles of 50. Each 5-ml. teaspoonful of reconstituted Granules or each Chewable tablet provides erythromycin ethyl succinate equivalent to 125 mg. of erythromycin activity and 167 mg. of each of sulfadiazine, sulfamerazine and sulfamethazine.

701358

## NATIONAL AND REGIONAL MEETINGS

**October 23: American Association of Poison Control Centers. Washington Hilton Hotel, Washington. Address: Dr. Matilda S. McIntire, Secretary, Children's Memorial Hospital, 44th and Dewey Avenue, Omaha, Nebr. 68105.**

October 25–28: American Clinical and Climatological Association. The Homestead, Hot Springs, Va. Address: Dr. F. T. Billings, Jr., Secretary-Treasurer, 420 Medical Arts Bldg., Nashville, Tenn.

October 27–30: Association of American Medical Colleges. New York Hilton Hotel, New York. Address: Dr. Robert C. Berson, Executive Director, 1501 New Hampshire Avenue, N.W., Washington, D. C. 20036.

October 29: American Association of Ophthalmology. Palmer House, Chicago. Address: Mr. Lawrence A. Zupan, Executive Secretary, 1100 17th Street, N.W., Washington, D. C. 20036.

October 29–November 3: American Academy of Ophthalmology and Otolaryngology. Palmer House, Chicago. Address: Dr. William L. Benedict, Executive Secretary, 15 Second Street, S.W., Rochester, Minn. 55901.

November 2–3: Conference on Aging and Long-term Care. The Emerson Hotel, Baltimore, Md. Address: Committee on Aging, American Medical Association, 535 North Dearborn Street, Chicago, Ill. 60610.

**November 2–5: Association of Clinical Scientists: "The Laboratory Diagnosis of Kidney Diseases." Hotel America, Washington. Address: Dr. Robert P. MacFate, Secretary-Treasurer, 300 North State Street, Chicago, Ill. 60610.**

**November 13–14: Seminar on Oral Communications in Medicine and Dentistry, sponsored by Smith Kline & French Laboratories. Marriott Key Bridge Motor Hotel, Arlington, Va. Address: Mr. Biagio J. Melloni, Chairman, Audio-Visual Teaching Committee, Georgetown University, Washington, D. C. 20007.**

November 13–16: Southern Medical Association. Miami Beach, Fla. Address: Mr. Robert F. Butts, Executive Director, 2601 Highland Avenue, Birmingham, Ala. 35205.

**November 19–22: Association of Military Surgeons of the United States. Sheraton-Park Hotel, Washington. Address: Brig. General Frank E. Wilson, USAR (Ret.), Executive Director, 1500 Massachusetts Avenue, N.W., Washington, D. C. 20005.**

**November 20–22: Annual Scientific Assembly, The Medical Society of the District of Columbia. Statler-Hilton Hotel, Washington. Address: Mr. George W. Cooley, Executive Director, 2007 Eye Street, N.W., Washington, D. C. 20006.**

November 26–29: American Medical Association (Clinical Convention). Houston, Texas. Address: Dr. F. J. L. Blasingame, Executive Vice President, 535 North Dearborn Street, Chicago, Ill. 60610.

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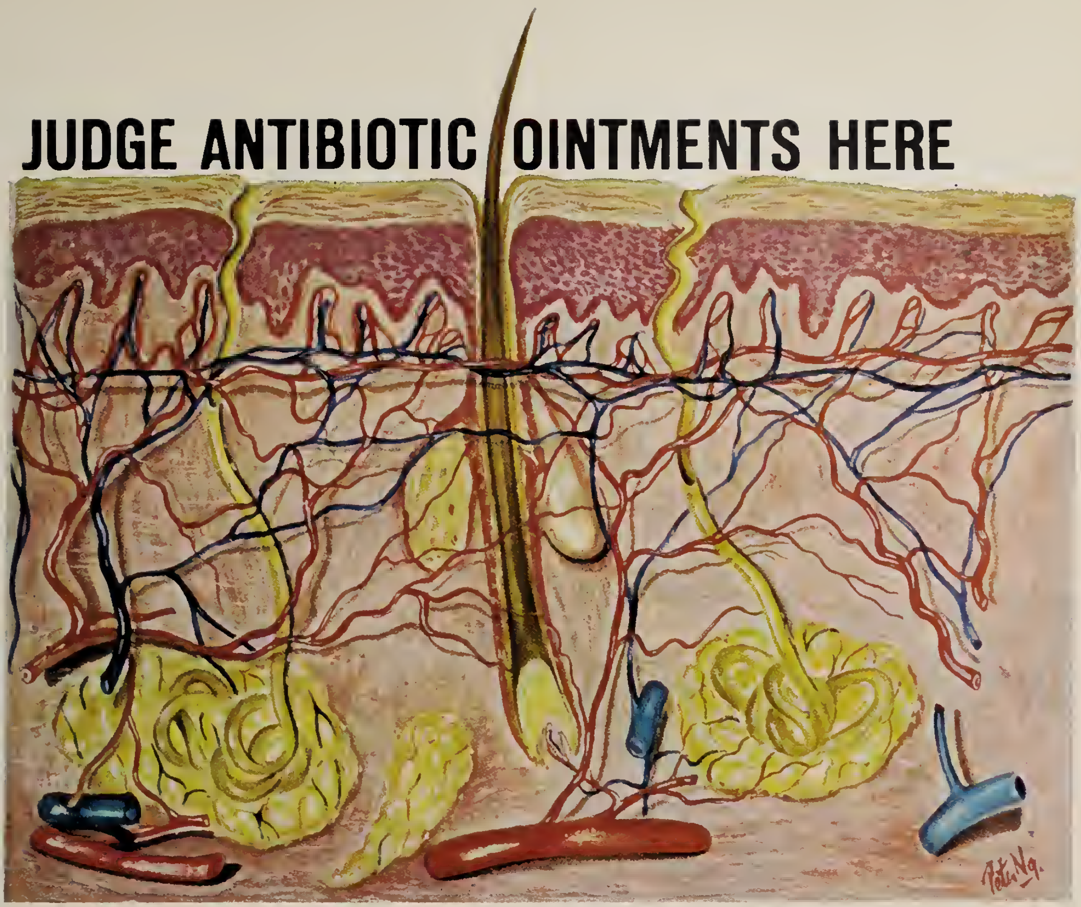

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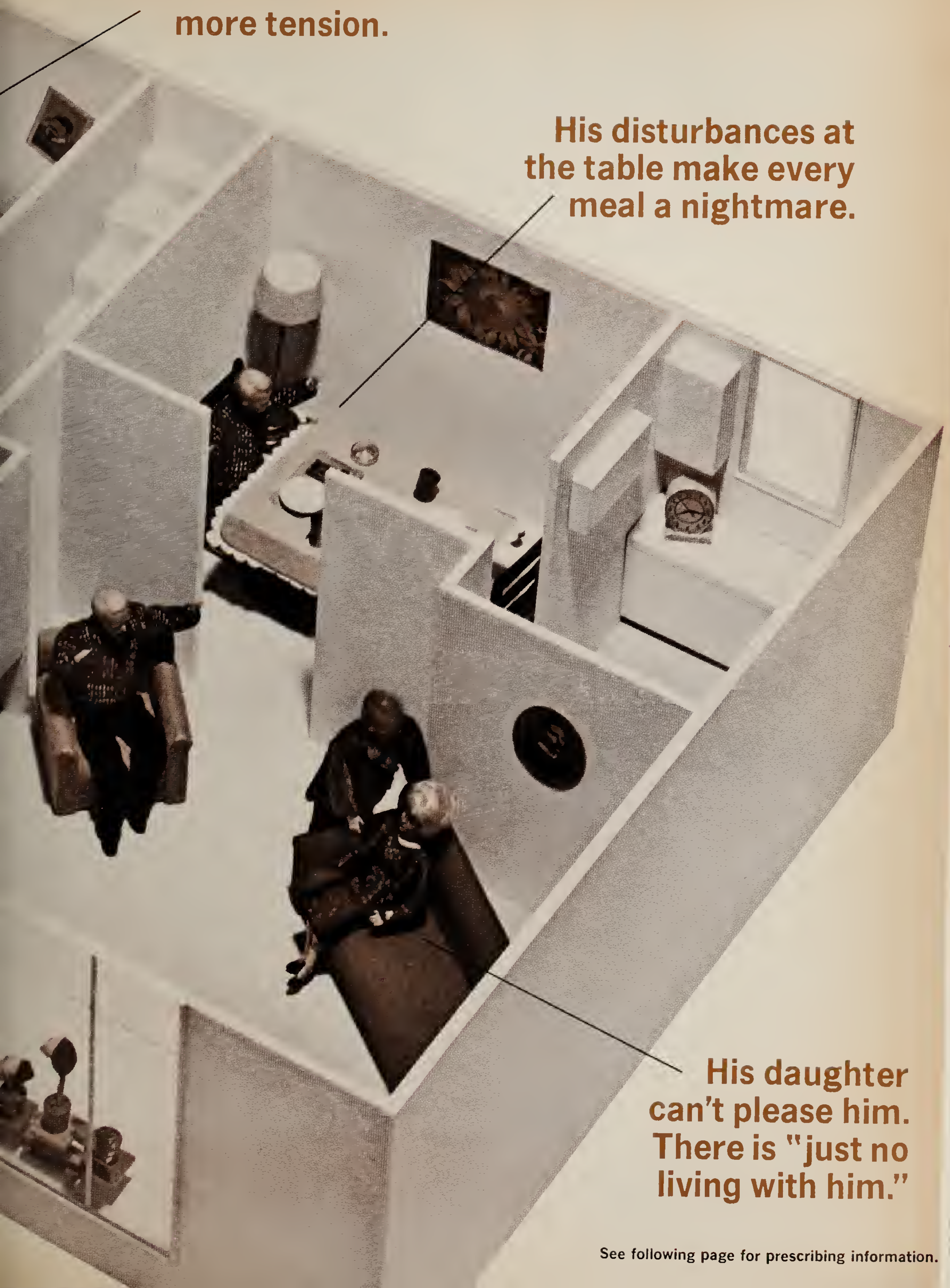

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*Warning:* If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

*Precautions:* Before prescribing, carefully select patients, avo those responsive to routine measures as well as contraindicatec tients. Obtain a detailed history and a complete physical and labor examination, including a blood count. The patient should not ex recommended dosage, should be closely supervised and shoul warned to discontinue the drug and report immediately if fever, throat, or mouth lesions (symptoms of blood dyscrasia); sudden w gain (water retention); skin reactions; black or tarry stools or evidence of intestinal hemorrhage occur. Make regular blood co Discontinue the drug immediately and institute countermeasures white count changes significantly, granulocytes decrease, or imm forms appear. Use greater care in the elderly and in hypertens

*Adverse Reactions:* The most common are nausea, edema and rash. Swelling of the ankles or face may be minimized by withho dietary salt, reduction in dosage or use of diuretics. In elderly pa and in those with hypertension the drug should be discontinued the appearance of edema. The drug has been associated with pept

**For 280-lb. tackles—or 108-lb. housewives—Butazolidin alka can hasten recovery from the agonizing pain of shoulder bursitis.**

**It's not for every patient. Check carefully the Contraindications, Warning and Precautions shown below.**

**And adverse reactions may occur. The most common are nausea, edema and rash. Rarely, agranulocytosis has been reported. All adverse reactions are listed below, too.**

**Play-for-pay or workaday patients—when they come up with shoulder bursitis and your clinical judgment indicates Butazolidin alka—go with it.**

**And watch the comeback.**

c and may reactivate a latent peptic ulcer. The patient should be in-
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w reduction of dosage. However, rash accompanied by fever or
ot r systemic reactions usually requires withholding medication.
P uric rash has also been reported. Agranulocytosis, exfoliative
d natitis, Stevens-Johnson syndrome, or a generalized allergic re-
a on similar to serum sickness may occur and require permanent
w drawal of medication. Stomatitis, salivary gland enlargement,
v iting, vertigo and languor may occur. Leukemia and leukemoid
re tions have been reported. While not definitely attributable to the
d , a causal relationship cannot be excluded. Thrombocytopenic
p ura and aplastic anemia may occur. Confusional states, agitation,
h dache, blurred vision, optic neuritis and transient hearing loss have
b n.reported, as have hyperglycemia, hepatitis, jaundice, and several
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**MEDICAL ANNALS**

*of the District of Columbia*

*October 1967* VOLUME XXXVI • NUMBER 10

# Rhythm of Sexual Desire in the Human Female

JOHN R. CAVANAGH, M.D., F.A.C.P.*

UNTIL APPROXIMATELY 50 YEARS AGO it was generally presumed that sexual feelings in the normal human female did not occur. If the normal woman had no sexual response, the presence of such a response was therefore abnormal. At the beginning of the present century the French Academy of Medicine came to the conclusion that a normal woman could and should be expected to have a sexual response during coitus. Although there is no longer any doubt that a woman may be expected to have such a response, its occurrence is not frequent (Kroger and Freed,[1] Brown and Kempton,[2] English,[3] and Kinsey[4]).

The interest of this paper, however, is not in orgiastic response but on a less known topic—whether or not there is a rhythm of sexual desire in the human female. Very few articles on this topic have appeared in the literature. Most of them appeared in the thirties at about the time that Ogino[5] and Knaus[6] published their findings on the periodicity of ovulation.

## Biologic Rhythms

Until recently very little was known of biologic rhythms. Clinicians have long recognized such physiologic rhythms as the menstrual cycle and the normal diurnal fluctuations in body temperature, but until recently the "biologic clock" phenomenon attracted mainly academic interest. During the past few years, however, scientists have discovered so many additional cycles, affecting such diverse functions as mitosis, heart rate, and drug reaction, that many investigators predict that current biorhythm research will exert a profound effect on clinical medicine in the near future. Under these circumstances a rhythm of sexual desire may be expected.[7]

One of the earliest studies of this subject was made by Stopes[8] of "happy wives" who were separated from their husbands by military duty. These women, of whom it was stated that they constantly longed for their husbands and desired their closeness in physical embrace, had periods in which they had an intense longing for sexual union. In this regard Stopes commented:

> "It is from such women that I got the first clue to the knowledge of what I call the law of Periodicity of Recurrence of Desire in women. For some years I have been making as scientific and detailed a study as possible of this extremely complex problem. Owing to the frank and scientific attitude of a number of women, and the ready and intimate confidence of many more, I have obtained a number of most interesting facts from which I think it is already possible to deduce a generalization which is illuminating, and may be of great medical and sociological value [Ibid., pp. 37–38]."

Stopes speculated on why it was that so few women were able to recall the various phases of sexual desire, if any, which occurred during the menstrual month. She concluded, with most of those who have studied the subject, that the uncertainty on the subject is due to a failure of women to devote adequate introspection to this concept. As a result of this, little attention has been paid to the scientific aspects of the problem. Stopes concluded that increased sexual desire occurred in the woman just after the menstrual period and in midcycle at about the time of ovulation. Most researchers agree with Stopes that increased sexual desire occurs in conjunction with the menstrual period. Biologically one would also expect increased sexual desire at the time of ovulation in order to help maintain the population.

If increased desire occurred at the time of ovulation it could readily be seen that those women who for religious reasons were restricted to the nonfertile periods would suffer severe frustration.

Stone and Stone[9] reported on this problem:

> "Furthermore, in all animal life the days of ovulation coincide with the period of greatest sexual desire. In

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many species, in fact, the female will accept the male only during her fertile period. It is likely that in the human female, too, there is an increased sexual interest during her ovulation time, and the observance of the 'safe period' which bars sexual relations at this time is a practice which is not always desirable or advisable from a psychosexual point of view [p. 107]."

## Review of the Literature

If we look at the literature on the subject there is general agreement that a peak or peaks of sexual desire do occur. Before discussing my own observations a brief review of the published articles on this subject may be helpful.

EXNER[10]: "In the great majority of women sex desire varies with the menstrual cycle. At certain periods in the cycle she is more easily aroused sexually than at other times, or specific desire may arise spontaneously without external stimulation. There occurs a tidal ebb and flow in sex desire which in some women is so marked and so regular that they can definitely locate its peak by date, in relation to menstruation, while other women recognize a periodicity in desire but are not conscious that these periods come with regularity. Other women do not recognize any periodicity at all [p. 69–70]."

Exner does not specifically limit this desire temporally. He states, however, that "if 2 such peaks of desire occur in many women, it can easily be seen what harm could result." Although it has been sought, no sexual periodicity has been found in men (Ibid., pp. 69–72).

STONE AND STONE[9]: "The degree of woman's erotic sensibility has long been a matter of considerable dispute. For a time it was seriously maintained that sex desire was primarily or entirely a masculine attribute and that woman was devoid of sexual feelings. Acton, a well-known English physician who was considered an authority on sex matters some fifty years ago, wrote that 'the majority of women, happily for society, are not much troubled with sexual feelings,' and that the supposition that women possessed any erotic desires was a 'vile aspersion.' Other writers of that period maintained a similar point of view. . . . After a rather exhaustive survey of this subject, Havelock Ellis comes to the conclusion that the sexual impulse is fairly well balanced between the two sexes. It is rather generally assumed at present that the woman's erotic desires are just as strong as those of the male, although the manifestations of the sexual urge may vary considerably in the two sexes [pp. 165–167]."

The following information is quoted verbatim from Dr. Hart's article[11] in the *British Medical Journal*:

HART[11]: "The more recent literature continues to show marked differences of opinion in regard to the rhythm of sexual desire. Thus Corner maintained that libido is maximal just before or just after menstruation, whereas Stopes considered the monthly rhythm to have two peaks, one just before menstruation and the other at midcycle. On the other hand, Eckstein and Zuckerman stated that 'sexual behavior in women very rarely manifests a rhythmic pattern' However, according to Swyer, 'Psychic changes occur throughout the menstrual cycle. So great are the variations in different individuals that generalizations are difficult to draw.'

"Table 1 shows that in 59 per cent of the patients the time of maximum libido was closely associated with that of menstruation. Only 6 per cent reported this maximum to be in the middle of the cycle and so at about the time of ovulation, when fertility would be expected to be maximal. In 34 per cent libido was not reported to be greater at any particular time of the menstrual cycle."

HOWELL[12]: "The sexual excitement that attends the condition (heat or estrus) in lower animals is not distinctly represented in man, although it is commonly said that in the period following menstruation the sexual desire is stronger than at other times."

MARSHALL[13]: "The period of most acute sexual feeling is generally just after the close of the menstrual period."

ELLIS[14]: "Whatever doubt may exist as to the most frequent state of the sexual emotions during the period of menstruation, there can be no doubt whatever that immediately before and immediately after—very commonly at both times—this varying slightly in different women, there is usually a marked heightening of actual desire."

Ellis quotes Kraft-Ebing who places the heightening of sexual emotion at the postmenstrual period, Adler who states that it is increased before, during and after menstruation, and Harry Campbell who, as a result of certain inquiries made of male patients at a London hospital, declared of their wives that the proportion of cases in which sexual feeling was increased after was 3 to 2.

DAVIS[15]: "In other words, desire occurred at 'less regular intervals.' In this group there were 201 women who placed their desire with reference to the menstrual period. Of these, 166 women stated that they were sometimes conscious of desire but not each month. When it did not come it preceded menstruation in 93 cases and followed in 40. Thirteen others said 'one or two,' 20 said 'two' and two sometimes experienced from one to three such periods."

Money[16] in 1965 commented on the study of Benedek and Rubenstein[17]:

"Cyclic fluctuation of sexual behavior in human partners relative to the menstrual cycle of the female has been investigated only by means of verbal report and from the woman only. Allowing for individual variation, the consensus has been that sexual desire in the active sense of taking the initiative has been strongest at the progestinic phase of the cycle, that is, around the time of the menstrual flow. The dissident opinion has been that of Benedek and Rubenstein who correlated psychoanalytic interpretation of free associative and dream material with vaginal-smear changes in 15 women. They identified the ovulatory, estrogenic phase of the cycle with active heterosexual tendencies, and the progestinic, menstrual phase with preparation for motherhood. In the light of Michael and Herbert's data, one wonders whether Benedek and Rubenstein may not better have described the ovulatory phase as one of sexual willingness and surrender to the approaches of the male, and the menstrual phase as one of greater initiative."

This study is important because it was an early attempt to correlate mental content and hormonic changes.

Kopp[18] asked 8,434 women, "Do menses affect desire?" He summarized the answers given to this question which are pertinent to this discussion:

"Judging from the above answers, most women are not sufficiently observant in personal matters to be able to give a definite answer to this question. Convincing answers might have been obtained if they had had time to observe themselves over a period of some months. By comparing the data in the Davis study on periodicity of desire, we find about 29 per cent of the unmarried women who answered the question reported that menses do not affect desire and 18 per cent in the group of married women, while we have 53 per cent in our cases against her 47 per cent. The higher grade of intelligence in the Davis group may account for greater accuracy in answers [pp. 97–99]."

Periodicity of sex desire with reference to the menstrual cycle was reported at regular intervals in 3,076 cases. Periodicity was observed as occurring once monthly in 2,539 cases, or 82.6 per cent; twice monthly in 471 cases, or 15.3 per cent; and 3 times monthly in 66 cases, or 2.1 per cent (p. 99).

Terman[19]: "Hamilton reports that only 19 of his 100 subjects deny rhythm, the period most frequently mentioned being just after menstruation. His data suggest that women who experience most intense desire at this time are more likely than others to be adequate as to orgasm. Contrary to Hamilton, Davis reports that for her unmarried group of 868 women the most frequently mentioned period of heightened sex feeling is just before menstruation. Our data support Hamilton as to the period most frequently named, but fail to show any appreciable relationship between rhythm and orgasm adequacy."

As stated above, estrus in animals is not comparable to menstruation in the human female.

Tinklepaugh[20]: "While woman ordinarily is sexually stimulable at any period of the menstrual cycle, present evidence may be interpreted as indicating that commonly she experiences 2 periods of heightened sex desire. One of these periods falls at the inappropriate time for reproduction, just prior to menstruation, the other occurs during the postmenstrua, prior to the period of ovulation and at the fertile period of the cycle. The time of occurrence of the second of these periods is in harmony with present knowledge of the mammalian sex cycle, but the first period is difficult to explain by any physiologic knowledge now available.

"At the human level there appear psychologic factors sufficiently marked to obscure partially what I believe is basically the same biological estrus cycle observed in lower animals. Most important of these in connection with the present problem is the sexual stimulability of the human female. That woman ordinarily may be stimulated to sexual receptivity at any time of the cycle and frequently is unaware, on the basis of retrospection, of any regularly occurring period of enhanced desire does not disprove the existence of such periods. Davis in her study of the sex lives of 2,200 women reports 272 unmarried and 126 married subjects who designated regular periods of sex desire. Some of these experienced one period, some two. The times of occurrence relative to menstruation, as placed by these women, including duplications by those reporting more than one period, were as follows:

| | *Before* | *During* | *After* | *Between or Midway* |
|---|---|---|---|---|
| Unmarried........ | 205 | 46 | 152 | 20 |
| Married.......... | 88 | 20 | 83 | 14 |

Dickinson[21] in 1927 collected, analyzed, and coördinated graphically on the basis of the menstrual cycle much of the available material concerning the reproductive cycle in woman. In this manner he was able to show a general correspondence between the much-questioned though frequently quoted "wave of well-being," variously attributed to van Ott, Reinl and Selheim, and the bimodal curve of sex desire secured by Davis, in each of which a primary crest occurs during the premenstrual week, followed by a drop during the flow, and a secondary crest during the postmenstrua.

McCance et al[22]: "The main peak was obviously on the eighth day, and this agrees reasonably well with the objective work which has been done on women and monkeys, and which has already been discussed. It is

> satisfactory that the greatest degree of desire should precede ovulation, but if, as Zuckerman (1936) maintains, the human sperm can rarely live in the female generative tract for more than 2 days, it is difficult to see why 7 days should elapse between the period of maximum desire in the female and her time of ovulation. On the other hand, many authors, reviewed by Hartman (1936), agree in considering the eighth day of the human cycle to be the most fertile. The evidence has been criticized by Hartman but is distinctly interesting in the light of the present results [p. 598]."

In married women the main peak was again on the eighth day, and these results indeed confirmed those of the single women in all important features (Ibid., p. 599).

The summary of these articles taken from the literature is shown in table 1. This indicates where each author places the peak or peaks of sexual desire.

**TABLE 1: Peak of Sexual Desire in the Human Female in Relation to the Menses by Various Authors**

| | Before | After | Midway |
|---|---|---|---|
| Corner | × | × | × |
| Stopes | × | | × |
| Swyer | | | |
| Hart | × | × | × |
| Howell | | × | |
| Marshall | | × | |
| Ellis | × | × | |
| Kraft-Ebing | | × | |
| Campbell | | × | |
| Davis | × | × | |
| Money | | | |
| Benedek | | × | |
| Kopp | × | × | |
| Terman | | | × |
| Hamilton | | × | |
| Beach | × | × | |
| Tinklepaugh | × | | × |
| Dickinson | × | × | |
| Cavanagh | | | × |
| | — | — | — |
| | 9 | 13 | 6 |

## Personal Investigation

My own interest in the peak of sexual desire arises out of giving advice on the use of the rhythm system for the control of conception. Many women asserted that their greatest sexual desire occurred during the fertile period. This was a source of frustration to them. In this regard it must be borne in mind that using The Rhythm according to the recommended "safe" way by the use of temperature requires abstinence in most cases from the first day of the cycle to the twenty-first to twenty-third day. In an effort to get information on a number of attitudes in regard to periodic abstinence a questionnaire was published in *Marriage Magazine*[23] in which the following question among others was asked:

> "9. It has been said that woman's greatest sexual desire is at the time of ovulation, during the 'unsafe' period for those practicing rhythm. (a) Was this true in your case? (b) If so, was it a source of frustration?"

The answers to these questions based on 580 replies were[24]:

| | *No.* | *Per cent* |
|---|---|---|
| 9—a. Total replies: 580 | | |
| Yes | 423 | 71 |
| Sometimes | 50 | 8 |
| No | 107 | 18 |
| 9—b. Total replies: 580 | | |
| Yes | 333 | 57 |
| Sometimes | 64 | 11 |
| No | 118 | 20 |
| No answer | 165 | 28 |

This response was interesting and at first seemed to confirm that for this group of women there was a decided increase in sexual desire at the time of ovulation. This conclusion can hardly be questioned, but the question might be raised as to whether this increased desire was due to deprivation of sexual activity or was a part of a basic rhythm of desire. These women were all deprived of sexual relations because of the use of periodic abstinence. It is well known, of course, that under normal circumstances abstinence "makes the heart grow fonder."

In an attempt to determine the regularity of such a basic sexual cycle it was decided to study the sexual rhythms of a group of women undergoing psychotherapy. It was believed that such women would in their dreams and expressed sexual feelings reveal a rhythm of sexual desire if such was present. Several difficulties immediately presented themselves. Some of the available subjects had had hysterectomies and there was nothing with which to compare the sex cycle; others were on The Pill, which by suppressing ovulation would also suppress desire if this is due to ovulation. Only those not having a sexual life could be used, because such activity would drain off sexual tension and do away with any peaks. Frigid patients were ruled out because by definition they had no conscious sexual desires. One such patient when asked about keeping a record of her sexual desires replied facetiously, "What are sexual desires?"

Another troublesome problem arose. Many

intelligent and happily married women apparently do not recognize their own sexual feelings. It was necessary, in otherwise willing subjects, to explain what feelings they would be expected to experience. When it was pointed out that such feelings would be expected to manifest themselves as sex dreams, a desire to be close to someone, genital sensations, a feeling of being feminine, and others, they expressed surprise. Some even believed that such sensations were sinful or "not nice."

Because of the difficulty of obtaining suitable subjects it was decided to study the sexual cycle of 15 individuals who seemed to meet the requirements. These were all unmarried girls who had a regular menstrual cycle. It was decided to report this study in the hope that more studies of this nature will be made.

At each visit the subject was asked to describe her sexual feelings and dreams which were recorded in relation to her menstrual cycle. To date these records reveal a pattern similar to that revealed in the literature. There was evidence of increased desire before and after the menses and pre-ovulatory. The degree of desire varied very much from the girl who said, "I always feel that way," to the other extreme of the girl whose reply was "nothing to report."

## Conclusion

This preliminary report seems to indicate that there are fluctuations in sexual desire in the human female which tend to follow a regular pattern. There is a consistent rise before and after the menses and in the pre-ovulatory period. There were, however, sexual feelings at other times of the month.

A more extensive study is under way by a group of collaborators, and it is hoped that this material will be available in the near future.

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*(Continued on page 650)*

# Maximum Terminal Air Flow

HALL G. CANTER, M.D.,* AND PETER C. LUCHSINGER, M.D.†

A BASIC DEFECT in most chronic respiratory diseases is ventilatory obstruction. This may be due to loss of lung elasticity, bronchospasm, retained secretions, or a combination of these. Functionally, this obstruction results in decreased flow of air into and, particularly, out of the lung.

A number of time intervals from the beginning of a forced expiration have been used as a basis of various tests of expiratory air-flow resistance. In spite of considerable standardization of terms, symbols and normal values, [1-4] their multiplicity has often led to confusion among clinicians. As measures of diffuse airway obstruction, the maximum expiratory flow rate (MEFR), the forced expiratory volume (FEV), the timed vital capacity (TVC), and the maximum midexpiratory flow (MMF) have been utilized. Each of these tests is measured entirely or partially during the first half of the forced vital capacity (FVC). They are dependent in part upon the patient's coöperation and effort and are influenced by extrathoracic airway resistance.

Based on theoretical considerations Hyatt and Fry[5] have shown that during the latter half of the vital capacity the relationship between maximum expiratory flow and lung volume is largely independent of effort and of resistance in the upper airways and is primarily determined by the physical properties of the lower airways of the lung. For these reasons a measure of air flow during the latter part of the expiratory volume should have clinical application.

A measure of flow after expiring three-quarters of the vital capacity has been used in this study to assess ventilatory dysfunction and has been given the name maximum terminal flow (MTF). While its value has been suggested on theoretical grounds, previous clinical analysis of its usefulness has been limited.[6]

The purpose of this study was to determine normal values for the maximum terminal flow (MTF) in a group of normal subjects as a function of age and size. Based on the normal values a prediction formula has been developed and used to assess ventilatory dysfunction in a group of patients with lung disease. Finally, the maximum terminal flow (MTF) has been compared to the maximum midexpiratory flow (MMF) in these patients to judge if MTF is superior to MMF as a measure of air-flow abnormality.

## Methods and Materials

A total of 447 adult male subjects were studied. Three hundred and twenty subjects had no evidence of lung disease, as judged by history, clinical examination, and chest X-ray films. They were selected from hospital employees, medical residents, staff physicians, and ambulatory patients with nonpulmonary disorders.

One hundred and twenty-seven patients with pulmonary diseases were studied. About one-half of these had chronic obstructive pulmonary disease (chronic bronchitis, obstructive emphysema), the remainder had various lung disorders which included interstitial diseases of the lung (sarcoidosis, interstitial fibrosis), inflammatory diseases (pneumonia, lung abscess), pleural diseases (empyema, pleural effusion), and bronchogenic carcinoma.

A Wedge spirometer (Model 170)‡ was used to determine volume and flow rates. This waterless spirometer offers virtually no resistance to breathing. It has a frequency response which is flat within 5 per cent up to 10 cycles per second. A loop plotting air flow against volume was displayed on the cathode ray oscilloscope of an Electronics for Medicine recorder.§ When the flow-volume loop showed a maximum envelope and was reproducible it was photographed. A curve from a normal subject is shown in figure 1.

The purpose of the test was explained and the method of testing demonstrated to each patient. All tests were performed in the upright position.

The major sources of error were excessive expiratory effort and air leakage. Excessive effort,

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§ Model DR8 Research Recorder, Electronics for Medicine, White Plains, New York.

particularly in emphysema, may result in transpulmonary pressures in excess of that required to produce maximum flow. For this reason all subjects were asked to exhale with varying degrees of effort, and the tracings showing maximum flow were measured. Air leakage was minimized by using a well-fitted mouth piece and by careful and repeated instruction. The instantaneous expiratory flow was determined at its peak value or maximum expiratory flow rate (MEFR), at one-half of the vital capacity or maximum midexpiratory flow (MMF), and after three-quarters of the vital capacity had been expired—maximum terminal flow (MTF).* Simultaneously with the instantaneous flow values the vital capacity was measured.

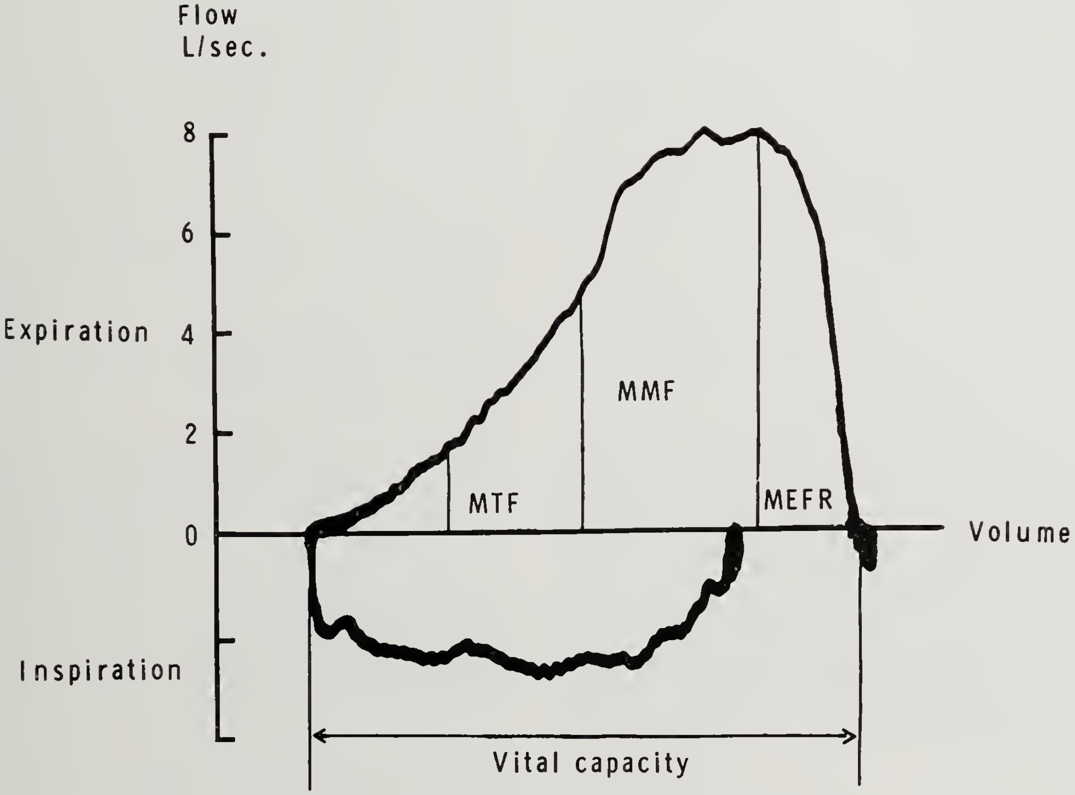

FIG. 1. Normal flow volume loop.

Information including the patient's age, race, diagnosis, cigarette consumption and predicted vital capacity as well as the observed vital capacity, maximum expiratory flow, maximum midexpiratory flow and maximum terminal flow was punched on IBM cards. The information obtained from the normal subjects was submitted to statistical analysis, which yielded normal values and ranges for each measurement. In addition, regression equations were developed which permitted calculation of predicted normal values for MEFR, MMF, and MTF as a function of age and the predicted vital capacity.

With the regression equations, MMF and MTF were predicted for each patient with lung disease, and these values were compared with the actual observed values and expressed as a ratio.

## Results

*Normal subjects.* The 320 normal subjects included 59 nonsmokers, 206 moderate smokers (less than 1 pack per day) and 55 heavy smokers (more than 1 pack per day). The mean age was 48.8 years, with a range from 19 to 74 years. Ventilatory function data on these subjects are listed in table 1. The average vital capacity is somewhat lower than predicted from the nomogram of Kory et al.[4] The expiratory flow rates fall within the range of normal reported in the literature. Analysis of the smoking histories revealed a median of 0.85 pack of cigarettes smoked per day for 23.25 years.

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* As indicated, the flow values in this study (MEFR, MMF and MTF) were determined instantaneously. The maximum expiratory flow rate (MEFR) and maximum midexpiratory flow (MMF) are also accepted to mean the volume of expired air per unit time measured between 200 and 1200 ml. volume of the forced expiratory vital capacity and the volume of air per unit time exhaled between 25 and 75 per cent of the forced vital capacity respectively.[4]

**TABLE 1: Ventilatory Function in 320 Normal Subjects**

| | Mean | SD |
|---|---|---|
| Vital capacity (VC) | 3.84 L | ±0.94 |
| Observed VC/Predicted VC | 0.85 | ±0.16 |
| MEFR | 6.33 L/sec. | ±1.83 |
| MMF | 3.61 L/sec. | ±0.32 |
| MTF | 1.48 L/sec. | ±0.62 |

The data were submitted to statistical analysis in order to compute linear regression equations for MEFR, MMF and MTF, using age, predicted vital capacity, observed vital capacity, and a combination of these parameters as independent variables. The regression equations which fitted best are as follows:

$$\text{MEFR} = 5.57 - .042\ \text{age} + .63\ \text{PVC}^*$$
$$\text{MMF} = 1.785 - .026\ \text{age} + .69\ \text{PVC}$$
$$\text{MTF} = 1.50 - .016\ \text{age} + .20\ \text{PVC}$$

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* PVC—predicted vital capacity.

The ages are of minor importance since they are already utilized in calculating the predicted vital capacity, but this age correction factor permitted an equation which fitted the data better than the use of the predicted vital capacity alone.

The ratio of observed to predicted value for each flow measurement was calculated with these prediction equations. These ratios are tabulated in table 2 for nonsmokers, moderate smokers, and heavy smokers.

**TABLE 2: Observed/Predicted Ratios in Smokers and Nonsmokers**

| | Nonsmokers (59) | Moderate Smokers (206) | Heavy Smokers (55) |
|---|---|---|---|
| Observed VC/Predicted VC | 0.91 | 0.84 | 0.82 |
| Observed MEFR/Predicted MEFR | 0.99 | 0.95 | 0.96 |
| Observed MMF/Predicted MMF | 1.13 | 0.99 | 0.86 |
| Observed MTF/Predicted MTF | 1.05 | 0.90 | 0.75 |

There is a progressive decrease in vital capacity and expiratory flow rates with increasing cigarette consumption. This difference between smokers and nonsmokers is not apparent in the MEFR determination but becomes obvious when the MMF is analyzed and even more apparent when the MTF is measured.

*Patients with lung disease.* This group consisted of patients with obstructive and nonobstructive lung diseases. MMF and MTF were measured in each patient. The predicted values were calculated and the ratio of observed to predicted value determined.

There were 14 patients with mild obstructive ventilatory defects. The vital capacity was normal in each (greater than 80 per cent predicted). The observed/predicted ratio averaged 0.66 for MMF and 0.67 for MTF. This indicates the similarity in the value of the 2 measurements. Furthermore, there was close agreement between the 2 tests in any individual patient.

More severe ventilatory obstruction was present in 48 patients whose average vital capacity was 61 per cent of predicted. In these patients the observed/predicted ratio for MMF was 0.27 and for MTF 0.31. Again no clear superiority of one measurement over the other was noted. If all patients with obstructive lung disease were considered together the difference between MMF and MTF was insignificant. As shown in table 3 the average observed/predicted ratio for MMF was 0.36 and for MTF 0.39.

**TABLE 3: Observed/Predicted Ratios in Patients with Lung Disease**

| | Nonobstructive Lung Disease | Obstructive Lung Disease |
|---|---|---|
| Observed VC/Predicted VC | 0.75 | 0.67 |
| Observed MMF/Predicted MMF | 0.69 | 0.36 |
| Observed MTF/Predicted MTF | 0.69 | 0.39 |

The group with nonobstructive lung diseases includes patients with pneumonia, pleural effusion, lung abscess, carcinoma of the lung, and other diseases not usually considered as causes of an obstructive ventilatory defect. There were 19 who had a normal vital capacity. The ratio of observed MMF/predicted MMF was 0.81 and for MTF was 0.87. Forty-three patients with nonobstructive lung disease had reduced vital capacities. The ratio of observed to predicted was 0.64 for MMF and 0.61 for MTF. These data are listed in table 3 and point out the similarity between MMF and MTF in patients with nonobstructive lung disease as well as obstructive disease.

## Discussion

The lung consists of air spaces and airways suspended in an elastic mesh. The elastic mesh is inserted between the outer surface of the airways (or air spaces) and the inner surface of the visceral pleura. On inspiration there is increased tension in the elastic mesh causing the intrathoracic airways to dilate. During expiration the tension in the mesh decreases, the airways become more narrow and air flow resistance increases, thereby decreasing expiratory air flow.

Numerous tests have been devised to evaluate disturbances in expiratory air flow. The time-volume relationship during the performance of the vital capacity has been used since its introduction by Tiffeneau and Pinelli[7] in 1948. More recently the maximal expiratory flow rate[5] and maximal midexpiratory flow[8] have become clinically useful. These measurements are made primarily during the first half of the forced expiratory vital capacity, i.e., at a lung volume where airway diameters are wide and alveoli still distended. Therefore, these measurements become primarily effort-dependent and also may be significantly influenced by upper airway resistance.

In 1958 Hyatt, Fry and Schilder[5] emphasized the important relationship between maximum expiratory flow and degree of lung inflation. They pointed out that at any given lung volume there is a maximum expiratory flow which cannot be exceeded regardless of effort. In fact, with excessive effort there may be decreased flow due to the increased pressure drop along the airway. This effect of decreased flow, resulting from effort in excess of that which is necessary to achieve maximum expiratory flow, is most apt to be manifested by patients with increased airway resistance, such as occurs in bronchitis and emphysema. The work of Hyatt, Fry and Schilder drew attention to the significance of measuring flow during the latter half of the expiratory vital capacity. The flow-volume relationship during this portion is less dependent on maximum effort, is minimally affected by variations in upper airway resistance, and should be a truer reflection of the physical properties of the intrapulmonary airways.[9]

In the present study expiratory flow was measured after three-fourths of the vital capacity had been exhaled. This measurement has been called maximum terminal flow (MTF). The test is easily obtained and quite reproducible. Although the respiratory flow-volume loop has been applied in epidemiologic surveys[6] no normal values for maximum terminal flow have been published. Therefore, normal values and ranges for adult men were first established and regression equations were developed which allowed predicted values to be calculated.

When observed flow rates were compared to the predicted values it was apparent that age and smoking habits influenced maximum terminal flow considerably. It was somewhat surprising to find that maximum expiratory flow rate (MEFR) was not influenced by smoking, even heavy smoking for many years (table 2). However, both the maximum midexpiratory flow (MMF) and maximum terminal flow (MTF) were lowered with increased smoking. This suggests that, in so-called normal subjects, airway dynamics during the latter half of the vital capacity may be altered even when peak expiratory flow in the first portion of the vital capacity is normal.

The second aim of the study was to determine if MTF had any advantage over MMF as a measure of airway dynamics in patients with lung disease. For this purpose 127 consecutive patients with lung disease were studied in the laboratory and both MMF and MTF measured as part of ventilatory function testing. A definite attempt was made to insure maximum expiratory flow throughout the expiratory vital capacity by repeated testing and instruction. The observed values for MTF and MMF were compared to the predicted values as calculated from the regression equations. No significant difference was detected between the 2 measurements (table 3). In patients with primarily obstructive lung disease the average MMF was 36 per cent of predicted, and the average MTF was 39 per cent. In patients with nonobstructive lung disease the average MMF and MTF were the same, 69 per cent of predicted.

The MMF and MTF are altered not only in diseases of the airways, such as bronchitis and emphysema, but also in diseases of the lung parenchyma and pleura. When there is obvious clinical evidence of airways obstruction the MTF does not add to the knowledge gained from the MMF. However, the MTF may be more sensitive in detecting subtle, subclinical evidences of decreased air flow and is therefore useful in epidemiological studies.

## Conclusions

Theoretical considerations suggest that measurements made during the latter half of the expiratory vital capacity may be more accurate reflections of the physical properties of the airways than measurements during the first half of expiration.

Maximum terminal flow (MTF) has been measured in 320 normal adult males after three-fourths of the vital capacity has been expired. Normal values for this measurement are published for the first time. Increasing age and especially increasing tobacco consumption influence MTF considerably.

In 127 patients with clinically obvious pulmonary disease, both obstructive and nonobstructive, the MTF and MMF were altered in the same direction and to the same degree. Both MTF and MMF appear superior to maximum expiratory flow rate (MEFR) in assessing airway dynamics.

The true role of MTF in ventilatory function testing awaits further application in larger groups of subjects. Its ability to detect subtle changes in air flow makes it useful in epidemiological surveys.

We gratefully acknowledge the assistance of Mr. Bert Levy and his staff for their assistance in the statistical analysis.

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## Cancer Patients Needed at Clinical Center

The coöperation of physicians is requested in continuing studies of cancer being conducted by the National Cancer Institute at the Clinical Center, National Institutes of Health, Bethesda, Md.

**Hodgkin's disease.** Particularly desired are patients who have had no previous treatment or minimal prior treatment. All clinical stages of biopsy-proven disease are acceptable. The major purpose of the study is to determine the curative potential of intensive radiotherapy in localized cases and to evaluate combination chemotherapy and X-irradiation in patients with generalized involvement.

**Chronic myelogenous leukemia.** Referrals of patients of all ages with high white blood cell counts and platelet counts are needed for studies of newer chemotherapeutic agents and as a source of white cells and platelets for in vitro and in vivo study.

Physicians who wish to have their patients considered for these studies may write or telephone Dr. Paul P. Carbone, Clinical Center, Room 12-N-226, National Institutes of Health, Bethesda, Md. 20014; telephone: (301) 656-4000, Ext. 64251.

**Carcinoma of the stomach or pancreas.** The National Cancer Institute's Radiation Branch is interested in the referral of patients with biopsy-proven, surgically unresectable carcinoma of the stomach or pancreas—particularly those with normal renal function and no history of hypertension or cardiovascular disease who have recently undergone an abdominal exploration and have completed their postoperative recovery.

Selected patients will be admitted to the Clinical Center as inpatients for the duration of their treatment (approximately 3 weeks), and subsequently will be rehospitalized as indicated for supportive care. Upon completion of their studies, patients will be returned to the care of the referring physician, who will receive a full report of the studies done.

Physicians and surgeons interested in having their patients considered for admission to this study may write or telephone Dr. Ralph E. Johnson, Clinical Center, Room B1-B-41B, National Institutes of Health, Bethesda, Md. 20014: telephone: (301) 656-4000, Ext. 65457.

# Treatment of Facial Fractures

LOUIS B. BALLA, M.D.*

THERE WERE 90 FACIAL FRACTURES admitted to the Washington Hospital Center between January 1, 1964 and December 31, 1965. The following fractures were treated:

- Blowout fracture of the orbit, 28 cases
- Fracture of zygoma or malar bone, 31 cases:
  - a. Combined fracture of the floor of the orbit, 15 cases
  - b. Zygoma and zygomatic arch fractures, 16 cases
- Zygomatic arch, 13 cases
- Contusion of the face and eye, 3 cases
- Maxilla, 8 cases
- Mandible, 7 cases

These fractures were treated by 4 departments:

- E.N.T., 34 cases (9 different physicians)
- Eye, 28 cases (18 physicians)
- Oral surgery, 15 cases (5 oral surgeons)
- Plastic surgery, 13 cases (2 physicians)

Fourteen are my own cases. The average hospital stay was 7 days; the shortest was 1 day (10 patients), and 1 patient stayed for 78 days, mainly because of a fractured femur and leg.

### Pure Blowout Fracture of the Orbit

This fracture, resulting from a blunt injury to the globe, involves only the floor of the orbit, leaving the infraorbital rim intact. Converse and Bell[1] have demonstrated the mechanism of the blowout fracture on cadavers. A blunt force pressing against the globe moves the globe posteriorly and the resulting increased pressure in the retro-ocular cone-shaped space can escape only through its weakest portion, the floor.[1-4]

The floor is triangular in shape, formed by the thin orbital plate of the maxilla, the zygomatic bone, and the orbital process of the palatine bone. The floor is weakened by the infraorbital sulcus which is covered only in its anterior portion. The infraorbital artery, vein and nerve run along the infraorbital sulcus and canal.

The mechanism and clinical findings are explained by the weak orbital floor:

- Diplopia (herniation of ocular muscles, evulsion of the third nerve)[5,6]
- Bleeding (intramuscular, retro-ocular, into maxillary sinus)[7]
- Dropping of orbital contents into the sinus[8]
- Subconjunctival hemorrhage or hyphema[4]
- Anesthesia or pain of face, lip[3]
- Enophthalmos or exophthalmos
- Laceration of the eye, intraocular bleeding

The diagnosis is made from the history, ocular examination, X-ray films (modified Water's view, linear laminography, polytomography or hypocycloid tomography, and orbitography).[9,10] In the differential diagnosis trauma of the eye and hematoma or cyst of the maxillary sinus should be considered.

Treatment consists of open reduction and subperiosteal insertion of an implant to the floor of the orbit (autogenous bone, cartilage, gelfoam, alloplastics),[5, 11, 12, 13] or elevation of the floor through the Caldwell-Luc procedure and packing of the sinus for 2 to 4 weeks.[7]

Twenty-eight patients were treated, and 25 surgical procedures were performed under general anesthesia. Twenty-four patients were treated by the Eye Department, 21 of them with open reduction and insertion of a polyethylene or silicone implant. Three patients were treated by otolaryngologists through the Caldwell-Luc approach and 1 by a combined Caldwell-Luc and insertion of a silicone implant. The injuries were the result of assault in 16 cases, a fall in 7, a car accident in 2, and sports injuries in 3.

### Fracture of the Zygoma or Malar Bone

Usually this is the result of a blow (fist, hard object) or other impact (fall, car accident) against the prominent cheek bone. The zygoma is a quadrilateral bone with a convex outer surface which forms the prominence of the cheek. It articulates with the frontal bone, maxilla, temporal bone, greater wing of the sphenoid and maxilla. It forms the greater portion of the lateral orbital wall. The maxillary sinus often extends into the zygoma at its upper lateral portion.

The type of injury depends on the direction of the impact. Commonly the zygoma is pushed medially and posteriorly, and a combined rotation is associated with the deformity. Often separation of the fronto-zygomatic suture line, fracture of the zygomatic arch, infraorbital rim, and maxillary sinus are found.

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The diagnosis is made from the history, inspection (ecchymosis of the periorbital tissues, eyelids, swelling of the cheek, depression of the zygoma, facial asymmetry), palpation (steplike depression of the infraorbital rim, separation of the frontozygomatic suture line, depression of the zygomatic arch), functional complaints (difficulty in opening the mouth, diplopia), and X-ray films (Water's view).

Treatment is by closed reduction (elevation and rocking of the zygoma into proper position with a towel clip), open reduction, intraoral approach (elevator inserted behind the tuberosity of the maxilla and pressure applied upward, outward, and forward), open reduction, Gillies' approach (incision of the skin over the hairline, an elevator inserted under the temporalis fascia down and forward to the zygoma and zygomatic arch for elevation), Caldwell-Luc approach (opening made into the anterior wall of the maxillary sinus, the zygoma elevated with a urethral sound and the sinus packed), incision over the eyebrow and internal wire fixation of the zygoma to the frontal bone, with incision over the infraorbital rim and internal wire fixation of the rim, and external traction (plaster of paris headcap and traction or halo head frame and traction).[1,14]

Thirty-one patients with zygomatic fractures were admitted and treated. In 15 cases a combined fracture of the floor of the orbit was present, and in 16 cases the zygomatic fracture was combined with the fracture of the zygomatic arch.

Of the 15 combined zygomatic and orbital floor fractures 14 cases were performed under general and 1 under local anesthesia. The Caldwell-Luc approach was used in 9 cases, open reduction with internal wire fixation and insertion of alloplastic (silicone, polyethylene) implant in 3 cases, a Caldwell-Luc and silicone implant in 1 case, open reduction and manipulation in 1 case, and no surgery in 1 case. One patient was treated first with open reduction and wiring of the zygomatic bone to the frontal bone and with the Caldwell-Luc and packing of the sinus. A few days later, after the decrease of the facial swelling, depression of the zygoma was still present. A second operation was performed and a plaster of paris headcap and external traction were applied to the depressed zygoma (figures 1 and 2). The injury was the result of assault in 8 cases, car accident in 5 cases, and a fall in 2 cases.

The 16 zygomatic and zygomatic arch fractures were all performed under general anesthesia. Open reduction and wiring was done in 9 cases, the Caldwell-Luc and Gillies' approach in 2 cases, the Caldwell-Luc and packing of the sinus in 2 cases, and closed reduction and elevation with towel clip in 3 cases. The injury was the result of assault in 7 cases, a fall in 6 cases, a car accident in 2 cases, and a football injury in 1 case.

### Fracture of the Zygomatic Arch

The zygomatic arch is formed by the zygomatic process of the temporalis and zygomatic bones. It contributes to the formation of the temporalis and zygomatic fossae. Its fracture is usually the result of an injury, such as a direct blow to the arch.

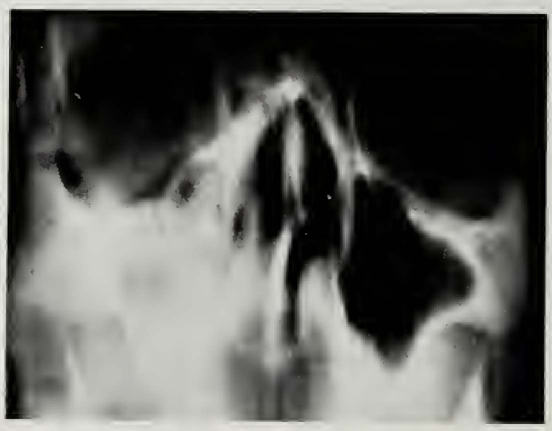

**FIG. 1.** Depression of right zygoma still present after wiring it to frontal bone and packing maxillary sinus.

The diagnosis is made from the history, inspection (depression, asymmetry, ecchymosis), palpation (depression, irregularity), dysfunction (difficulty in opening of the mouth by blockage of the coronoid process), and X-ray films (submental-vertex view).

Treatment is by closed reduction (elevation with towel clip), open reduction with an intra-oral approach, open reduction by the Gillies' approach, and open reduction and wiring of fragments.

Thirteen patients were treated, 11 under general and 2 under local anesthesia. The fracture was reduced with the Gillies' approach in 9 cases, closed reduction with towel clip in 2 cases, open reduction by the intra-oral approach in 1 case, and the Gillies' approach and wiring in 1 case. The injuries were the result of assault in 6 cases, a fall in 6 cases, and a football injury in 1 case.

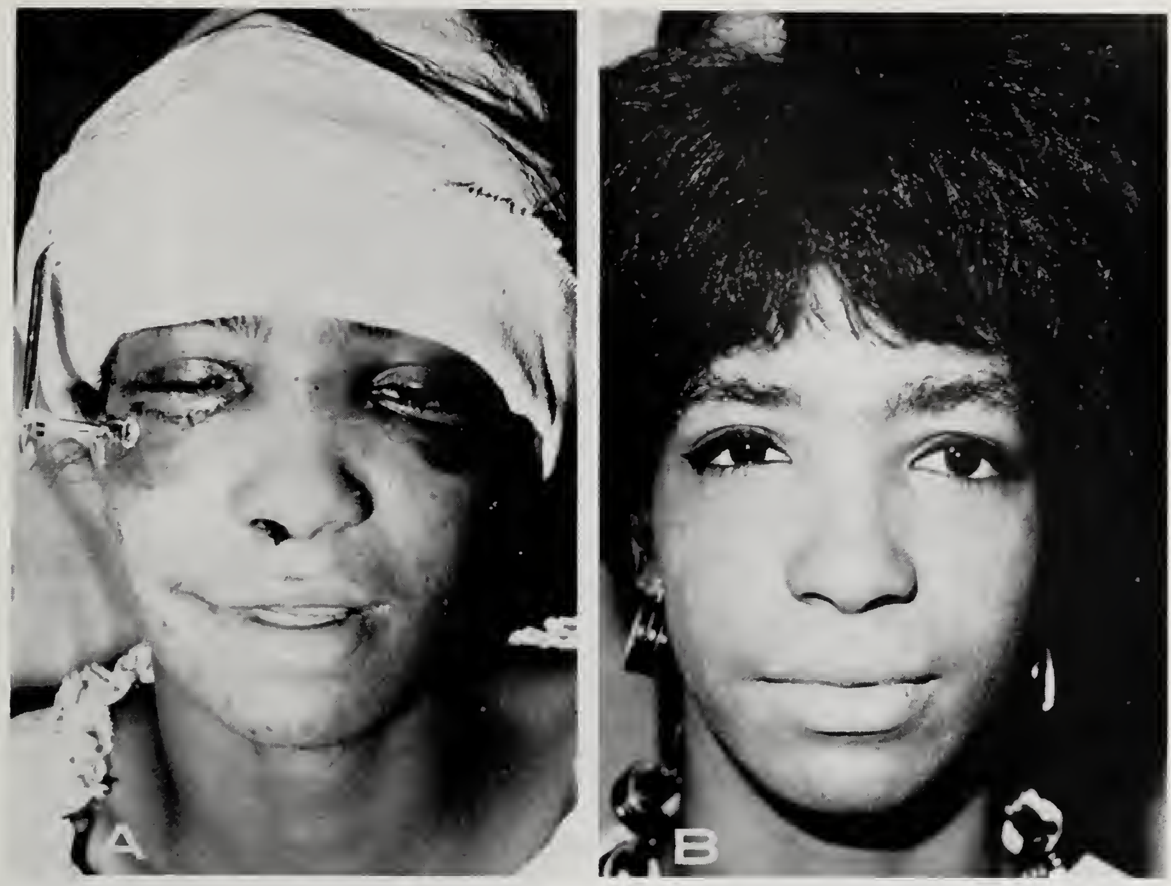

FIG. 2. A. Plaster of paris headcap and traction on depressed zygoma. B. Six months after surgery.

### Contusion of the Face and Eye

Three patients were admitted with contusion of the face and eye. Two of them received conservative treatment. One of them underwent an emergency operation shortly after admission with a gunshot wound of the maxillary sinus and floor of the orbit. Severe bleeding from the injured infraorbital artery was controlled during the surgery, which rapidly created temporary blindness and shock condition.

### Fracture of the Maxilla

This fracture is divided into 3 major portions:

Le Fort I or Guérin fracture (transverse fracture of the maxilla just above the teeth and alveolar ridge, palate, pterygoid process, and sphenoid bone).

Le Fort II or pyramidal fracture (nasal bones, frontal process of the maxilla, lacrimal bones, inferior rim of the orbit, floor of the orbit, zygomaticomaxillary suture, pterygoid plates, and pterygomaxillary fossa involved in the fracture line).

Le Fort III or craniofacial disjunction (complete separation of the facial bones from their cranial attachments).[4]

These fractures are usually the result of a car accident (typical in a dashboard injury) or severe beatings.

The diagnosis is made from the history, inspection (marked swelling and ecchymosis of the face and eyelids), palpation (various bony fractures and floating maxilla), dysfunction (malocclusion, trismus, nasal obstruction, diplopia) and X-ray films (Water's submental-vertex, and skull views).

Treatment is by closed reduction (interdental and intermaxillary wire ligatures, Erich arch bar) or open reduction and internal wire fixation.

Five patients with Le Fort I maxillary fractures were admitted and treated. Two were treated with interdental wire fixation, 1 with revision and open reduction and wiring, 1 with a revision and insertion of a silicone implant for cosmetic purpose, and 1 without surgery. Three injuries were the result of assault and 2 of car accident. One Le Fort II fracture was treated with open reduction and internal wire fixation. This was the result of a car accident. Two Le Fort III fractures were treated with open reduction and internal wire fixation. One of them was the victim of an assault, the other of a car accident (figures 3–6).

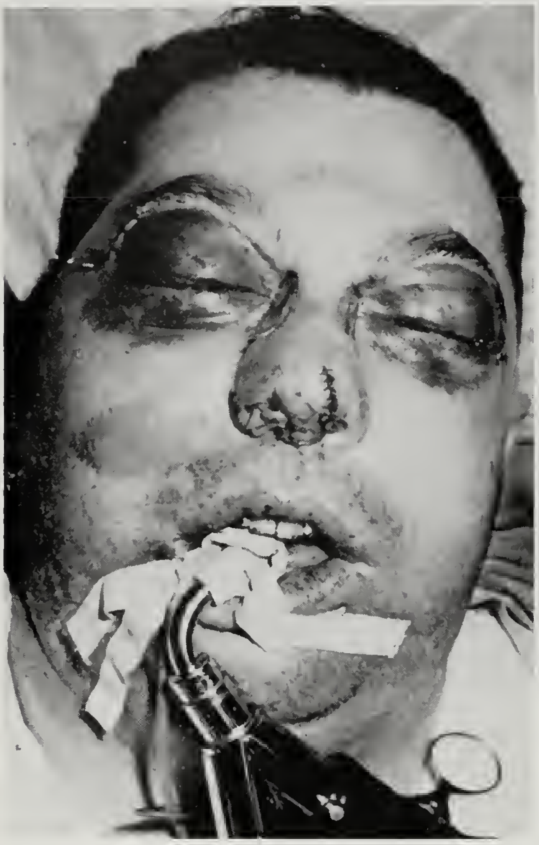

**FIG. 3. Craniofacial disjunction at end of reduction.**

## Fracture of the Mandible

This prominent part of the head is exposed to various traumatic forces. The 3 frequent sites of fracture are the condyle, the angle, and the horizontal ramus.

The diagnosis is made from the history, inspection (swelling, ecchymosis), palpation (fracture site felt, crepitus of fragments), dysfunction (malocclusion, trismus) and X-ray films (anteroposterior, lateral and oblique views).

Treatment is by closed reduction (interdental and intermaxillary wire ligatures, Erich arch bars, various prosthetic devices) or open reduction and wiring of the fragments.

Seven patients were admitted and treated, 6 with closed reduction and 1 with open reduction and wiring. Three were the result of assault, 2 of a fall, and 2 of car accidents.

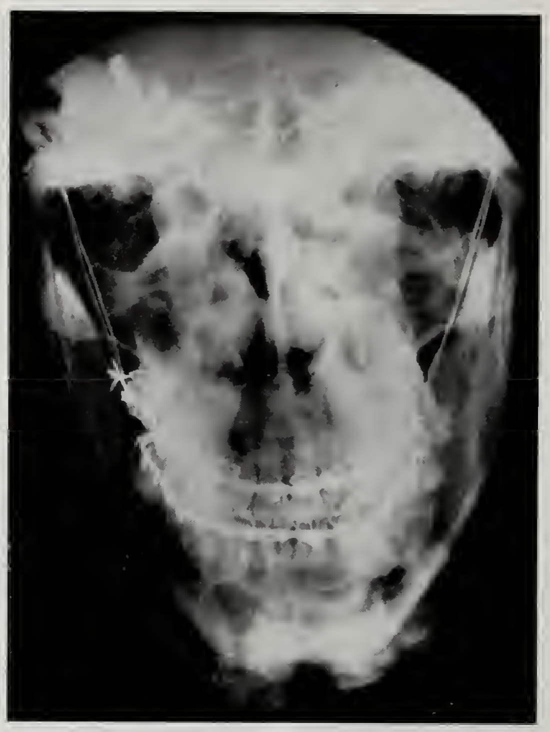

**FIG. 4. Postoperative X-ray film showing Erich arch bars and internal wire fixation from arch bars, fixing maxilla to frontal bones.**

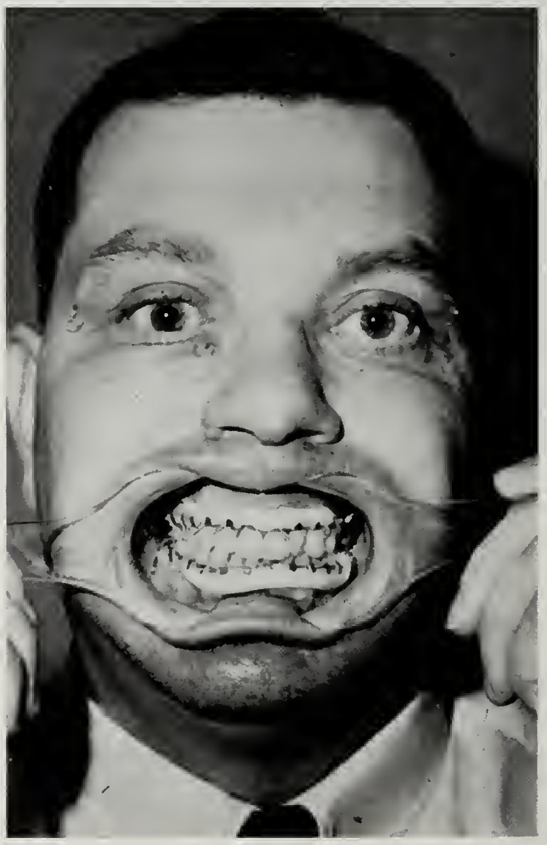

**FIG. 5. Four weeks postoperatively: Erich arch bars in place and teeth in perfect occlusion.**

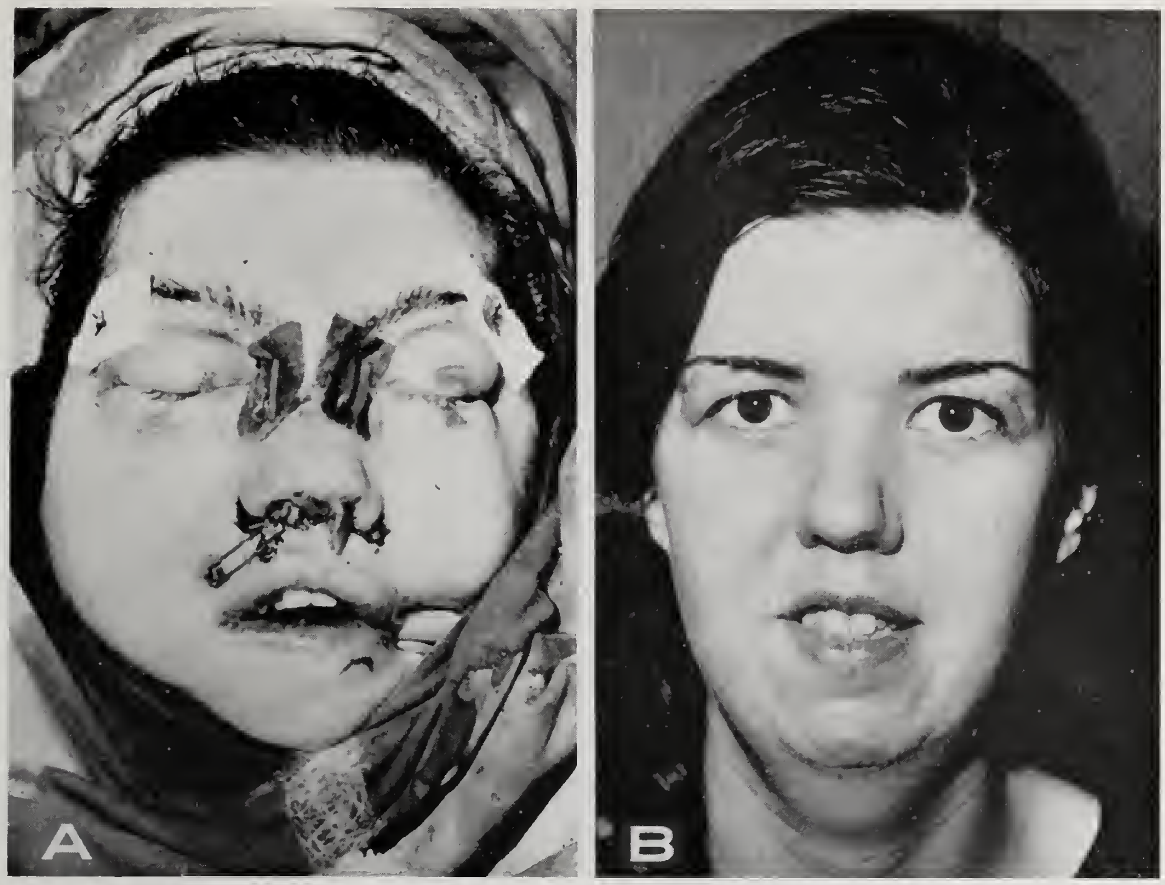

**FIG. 6. A. Craniofacial disjunction at end of operation. B. Three months after surgery.**

## Summary

Ninety common facial fractures were treated by 4 specialty departments with excellent results. One enucleation due to direct injury to the eye was performed. The various surgical methods correspond to the latest treatments reported and published in the medical literature.

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# Silent Mitral Stenosis Presenting as Pulmonary Hypertension with Right Heart Failure

MYRON L. LENKIN, M.D., * AND GERALD I. SHUGOLL, M.D., F.A.C.P.†

THE GREAT SYMPTOMATIC and hemodynamic benefits afforded patients with surgically correctable mitral stenosis make it essential for the clinician to diagnose accurately this condition. The fact that murmurs of valvular disease may disappear when the disease advances has been known since 1832. The English physician James Houk in 1832 described the murmurs as follows[1]:

"... Murmurs are not, as is often supposed, louder, *ceteris paribus*, in proportion as the valvular contraction is greater. On the contrary, the loudest murmurs are produced by a moderate contraction, and they become weak when it is extreme.... A contraction of the mitral or the tricuspid valve after only two, three, or four lines (one line equals one-twelfth of an inch) in diameter, I have frequently known occasion little or no murmur...."

In 1854 Hérard[2] recognized the fact that the diastolic murmur of mitral stenosis sometimes disappears during congestive heart failure. The following 2 cases are presented as illustrative examples of this entity.

## Report of Cases

**Case 1.** R. H. P., a 44-year-old white man, was referred to the Veterans Administration Hospital, Washington, D. C. for evaluation of chronic lung disease and pulmonary fibrosis. His complaints were dyspnea at rest and ankle edema of approximately 6 months' duration. Approximately 2 months prior to admission he began to cough up blood-streaked sputum. During 10 years prior to admission he had experienced several episodes of exertional syncope. He denied any knowledge of heart trouble or of rheumatic fever. Physical examination revealed an acutely dyspneic man with a blood pressure of 104/75 in both arms. He had distended cervical veins with a prominent A wave in his jugular venous pulse. There was increase in the PA diameter of the chest with bilateral basal rales. Pulmonary closure was accentuated and normally split, and there was a moderate right ventricular lift. The right ventricle occupied the apex. The first heart sound was of normal intensity. Murmurs were not heard. The liver was palpated 3 fingerbreadths below the right costal margin, and there was 4+ pitting edema extending to his knees bilaterally.

An electrocardiogram revealed normal sinus rhythm, right axis deviation with right ventricular hypertrophy, and left atrial enlargement (figure 1). A chest X-ray film revealed mild cardiomegaly with evidence of pulmonary venous congestion. There was evidence of left atrial enlargement and a prominent left atrial appendage. The main pulmonary artery was enlarged, and Kerley B lines were present (figure 2-A). Fluoroscopy revealed calcification of the mitral valve (figure 2-B). Cardiac catheterization was performed shortly after admission. The mean diastolic gradient across the mitral valve was 23 mm. Hg, resting right ventricular pressure 80/60 with simultaneous aortic pressure 97/75, cardiac output 2.6 L/min., cardiac index 1.6 L/min./M$^2$, and the calculated mitral valve area size 0.4 cm.$^2$

The patient refused cardiac surgery and was discharged to be followed in the clinic. His subsequent course over the next 6 months was characterized by recurrent episodes of biventricular failure. During several of his clinic visits an opening snap and faint diastolic rumble were heard when he was better compensated. On several occasions when he was noted to be in severe right ventricular failure a holosystolic murmur developed medial to the left sternal border which increased with inspiration and which was thought to represent tricuspid regurgitation. The course was progressively downhill, and the patient died in congestive heart failure several months later. At autopsy the mitral valve was found to be severely stenotic and heavily calcified. There were marked pulmonary atherosclerosis, anterior myocardial fibrosis, evidence of old pulmonary emboli, and passive congestion of his lungs and liver.

*Comment.* This patient with a potentially correctable valve lesion was thought by previous examiners to be suffering from lung disease with cor pulmonale. His physical findings were those of pulmonary hypertension with right heart failure. No auscultatory features of mitral stenosis were initially present. Left atrial enlargement on electrocardiogram and X-ray film was the first

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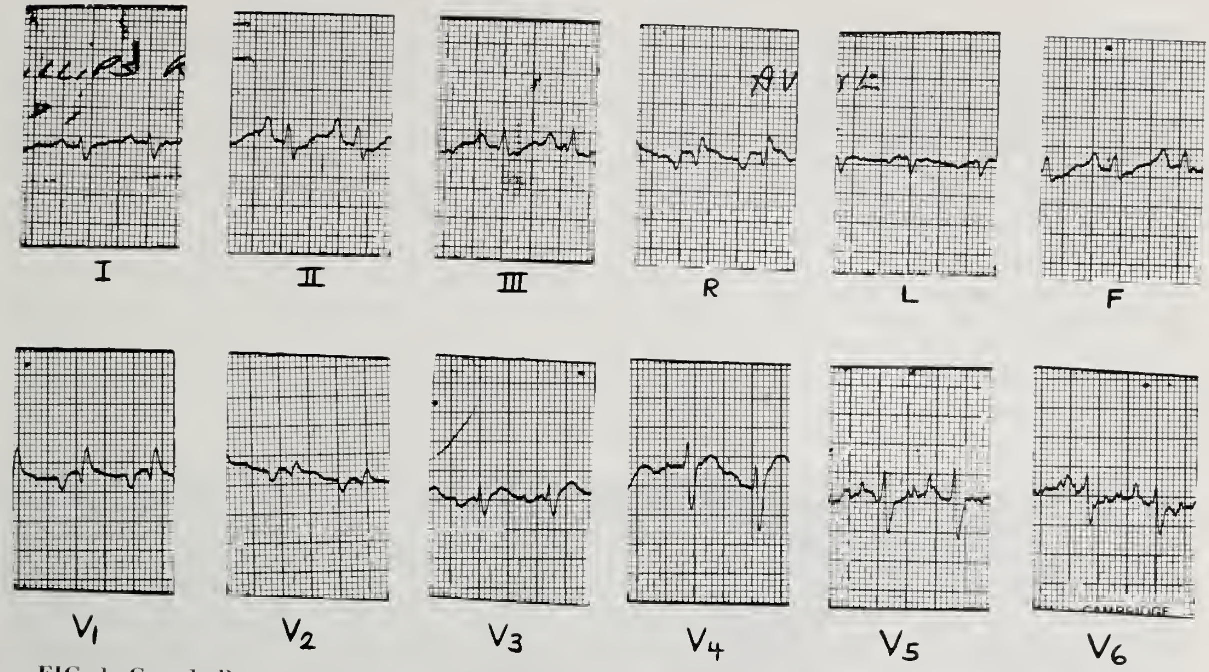

**FIG. 1.** Case 1. P waves consistent with left atrial enlargement. Early right ventricular hypertrophy is also present.

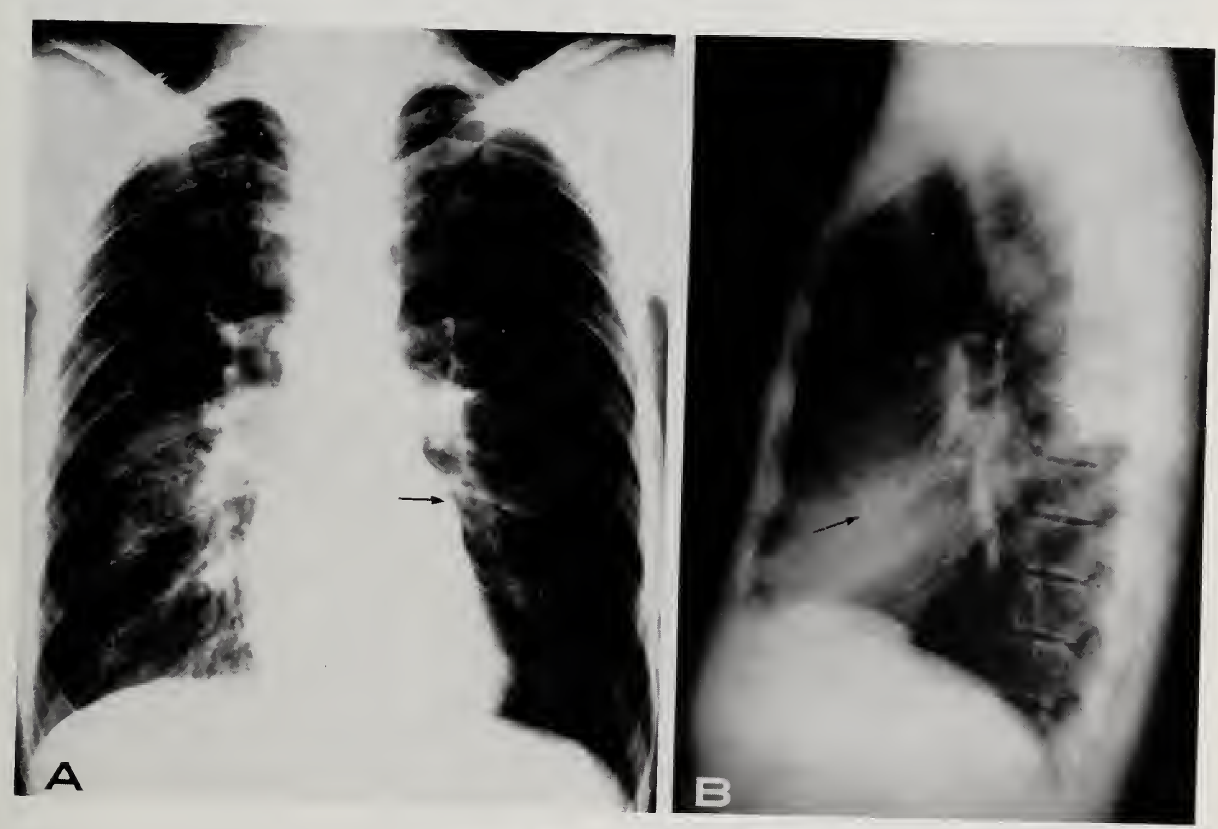

**FIG. 2.** Case 1. (A)PA X-ray film of the chest showing prominent pulmonary arteries and enlarged left atrial appendage (→). (B)Lateral X-ray film showing calcified mitral valve (→).

clue to the true diagnosis, supported by Kerley B lines and mitral calcification. Cardiac catheterization confirmed the diagnosis. Of note was the intermittent appearance of an apical diastolic rumble when cardiac output was improved by treatment of the heart failure.

**Case 2.** P. Mc., a 50-year-old white man, was transferred to the Veterans Administration Hospital, Washington, D. C. for cardiac evaluation. At the age of 5 years he was said to have had rheumatic fever, but he had no knowledge or symptoms of heart disease until approximately 4 years prior to admission when he developed dyspnea on exertion, paroxysmal nocturnal dyspnea, slight orthopnea, and ankle edema and was started on digitalis. Symptoms became progressively worse, and he was almost totally incapacitated during the 6 months prior to admission. He denied hemoptysis, fever, chills or arthralgia, but complained of occasional retrosternal pain which radiated toward the left elbow and appeared to be related to slight exertion and relieved by rest and nitroglycerine.

Physical examination revealed a depressed asthenic man appearing chronically ill. The cervical veins were distended to the angle of the mandible with a prominent V wave and positive H-J reflux. There was a prominent right ventricular lift with atrial fibrillation. The first heart sound was variable in intensity and somewhat diminished. Pulmonary closure was increased. There was a grade III/VI harsh holosystolic murmur heard along the lower left sternal border which did not change significantly with respiration and was thought to represent tricuspid regurgitation. No diastolic rumble was heard after careful listening over the apex in the left lateral decubitus position. After inhalation of amyl nitrite a short diastolic rumble could be heard at the apex. The liver was palpated 2 fingerbreadths below the right costal margin, and there was 1+ pretibial edema.

A chest X-ray film revealed the cardiac silhouette to be slightly enlarged with left atrial enlargement (figure 3-B). The pulmonary artery was quite prominent and Kerley B lines were seen at the right lung base (figure 3-A). Calcification of the mitral valve was noted. An electrocardiogram revealed early right ventricular hypertrophy and atrial fibrillation (figure 4). Subsequently after treatment for congestive heart failure a grade I/VI diastolic rumble could be heard intermittently at the apex. On catheterization the cardiac output was found to be markedly diminished (2.0 L/min.) The pulmonary arterial pressure was extremely high (102/64) exceeding systemic pressure (77/60 mm. Hg) with marked elevation of the pulmonary vascular resistance (24 Wood units). The pulmonary capillary pressure was also greatly elevated (28 mm. Hg) with a large vasoconstrictive component present as evidenced by response to oxygen and acetylcholine. A mean diastolic gradient (17 mm. Hg) produced a calculated mitral valve area which was extremely small (0.4 cm.$^2$). Cine-aortogram revealed mild aortic regurgitation and unobstructed coronary arteries.

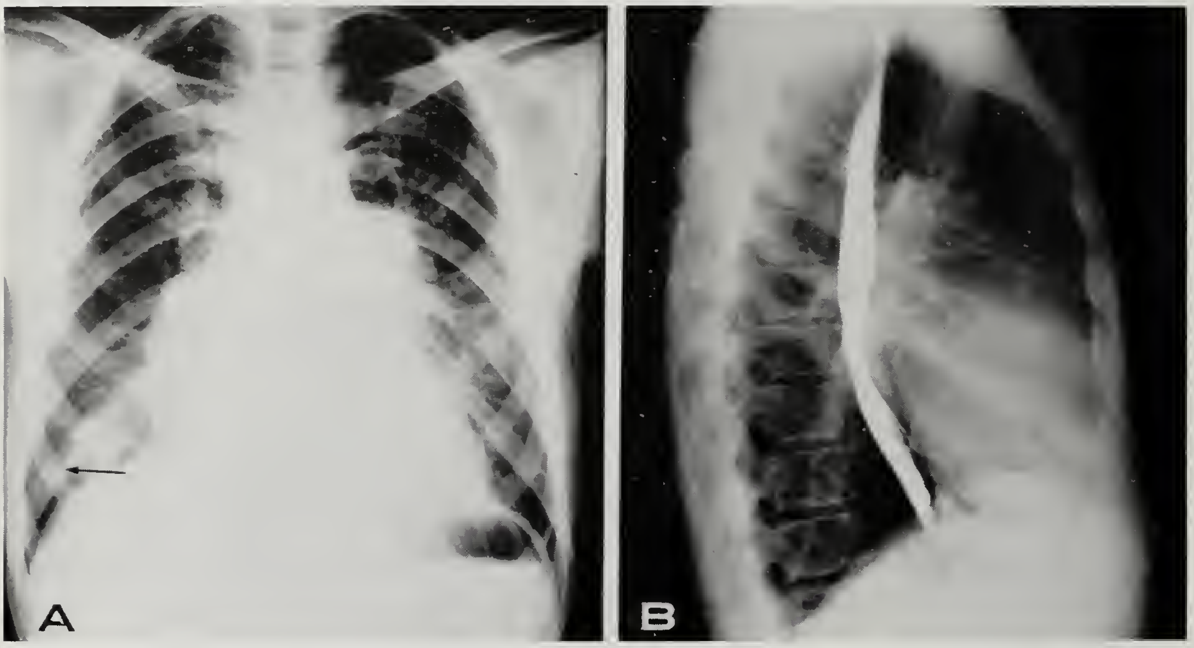

**FIG. 3. Case 2. (A) PA chest X-ray film showing large pulmonary arteries, large left atrial appendage, right ventricular enlargement, pulmonary venous engorgement, and Kerley B lines (←). (B) Lateral X-ray film demonstrating typical indentation of barium-filled esophagus by moderately enlarged left atrium.**

The patient underwent open heart surgery, and after an unsuccessful attempt at commissurotomy the mitral valve was replaced with a Starr-Edwards prosthesis. At surgery the mitral valve was found to be heavily calcified and severely stenotic. There was a large amount of thrombus material in the dilated left atrium. Postoperatively the patient remained comatose and died on the second postoperative day. At autopsy severe pulmonary atherosclerosis with mural thrombi in the main pulmonary artery and moderate coronary atherosclerosis were found. The prosthetic valve was intact. There was marked congestion of the liver and lungs. There was evidence of softening of the left parietal region of the brain.

*Comment.* Although the patient had a history of rheumatic fever there was initial doubt about his diagnosis because physical findings were those of pulmonary hypertension with right heart failure and tricuspid regurgitation. Left atrial enlargement, Kerley B lines, and mitral valve calcification on X-ray film provided the clues to the correct diagnosis. A mitral rumble could be elicited by the inhalation of amyl nitrite and, as in patient 1, could be heard after improvement in cardiac status by treatment of the heart failure. A loud first heart sound and mitral opening snap were also absent probably because of the heavily calcified immobile valve.

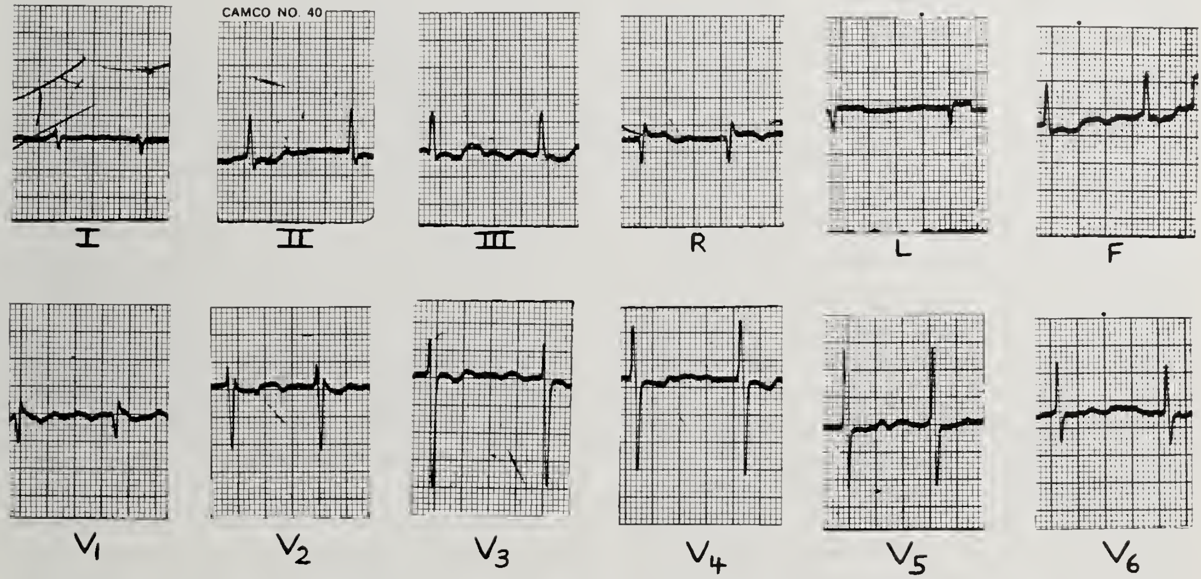

**FIG. 4. Case 2. Atrial fibrillation and evidence of early right ventricular hypertrophy.**

### Discussion

The auscultatory findings in the typical case of mitral stenosis include a prominent first sound, an opening snap, and a mid or late apical diastolic murmur. The duration, quality, and intensity of the diastolic murmur of mitral stenosis are determined by the degree of valvular deformity, the size of the valve orifice, the pressure proximal to the valve, and the volume and velocity of blood flow across the orifice. When patients are in congestive heart failure occasionally no murmur can be heard because of low flow across the mitral valve. When severe pulmonary vascular disease develops the murmur may be considerably diminished. Among 6 cases of mitral stenosis with very high pulmonary vascular resistance reported by MacKinnon, Wade and Vickers[3] there was no diastolic murmur in 3. Ravin[4] described an interesting patient with myxedema and mitral stenosis in whom the latter diagnosis was not made until the myxedema was treated and mitral flow increased.

In addition to the above factors, extra cardiac factors such as thickness of the chest wall and the proximity of the cardiac apex to the chest wall effect the transmission of the murmur. In patients with emphysema, severe obesity, and those with severe left-sided pleural effusion, one may not appreciate the murmur of mitral stenosis due to the impaired transmission of the sound and also because of the fact that the apex is displaced. It is of most importance that one locate the left ventricular impulse because the diastolic rumble is almost always heard best in this location. Those extrinsic factors may make it more difficult to hear the murmur, but this is not true silent mitral stenosis since the murmur can be demonstrated by intracardiac phonocardiography. Inhalation of amyl nitrite by causing increased flow and velocity across the mitral valve may accentuate a faint diastolic rumble.[5] A negative response, however, does not exclude mitral stenosis.

Severe pulmonary vascular obstruction can produce genuine silent mitral stenosis. Such cases are almost always associated with extremely tight mitral stenosis, low cardiac output, and right ventricular enlargement. This picture occurs only in a small percentage of patients with mitral stenosis in whom the pulmonary arterioles constrict and later hypertrophy with resultant extreme elevation of the pulmonary vascular resistance and pulmonary artery pressure. MacKinnon et al[3] found this to be true in 5 to 10 per cent of patients requiring mitral valvulotomy, and this agreed with the incidence (7.6 per cent) found by Wood[6] in 1952. In this series tight mitral stenosis was a constant finding, the valve size being estimated as less than 0.5 cm. in 4 out of the 5 patients.

The association of massive left atrial thrombosis with silent mitral stenosis has been reported.[7,8] It may be that in advanced stages of mitral stenosis when there is greatly diminished blood flow across the mitral valve stagnation of blood occurs in the dilated left atrium, and thrombosis is encouraged.

In general, patients with this entity seem to deteriorate more rapidly from the onset of symptoms. Their symptoms usually consist of exertional dyspnea, orthopnea, paroxysmal dyspnea, and hemoptysis. Despite the tight mitral stenosis, symptoms of pulmonary venous congestion may not predominate, and symptoms may be more related to the effect of the diminished cardiac output, i.e., extreme exhaustion, fatigue, exertional syncope, and occasionally angina. Stuckey[9] in 1955 suggested that angina occurs as a result of inadequate coronary blood flow during exercise because of fixed low cardiac output. It has been thought that the pulmonary hypertension and the low fixed cardiac output may protect the pulmonary capillary bed from hypervolemia, but signs of right heart failure may be manifest. A striking feature in this group of patients is the early onset of congestive heart failure and its resistance to intensive treatment.

Physical examination almost invariably reveals signs of pulmonary hypertension. The murmur of mitral stenosis may not be heard at all or may be heard intermittently from one day to the next. Thus, if a single examination fails to reveal a typical murmur one should follow the patient carefully because it may be detected later.[10] The absence of the murmur is related to diminished blood flow across the stenotic mitral valve and changes with varying degrees of cardiac decompensation. It may be that the enlargement of the right ventricle which may occupy the cardiac apex, pushing the left ventricle posteriorly, compounds the difficulty in hearing the murmur. Sinus tachycardia appears to be encountered in this group of patients more commonly than is atrial fibrillation.[3, 7, 10] Palpation reveals a right ventricular lift and a loud closure of the pulmonary valve. Frequently on auscultation the murmur of tricuspid regurgitation and the murmur of pulmonary regurgitation may be heard. The first heart sound and opening snap are variable. If the mitral valve is severely calcified and its motion restricted the first sound may be diminished, and the opening snap may be absent. Thus the physical findings related to pulmonary hypertension predominate with little or no evidence to suggest mitral stenosis.

The electrocardiogram indicates right ventricular hypertrophy and left atrial enlargement (or atrial fibrillation) with right axis deviation. X-ray examination and fluoroscopy of the heart may be especially helpful. The typical findings include an enlarged left atrium, prominent pulmonary arteries, and right ventricular enlargement. The peripheral pulmonary circulation may actually appear diminished. Kerley B lines and engorgement of the superior pulmonary veins indicate passive congestion. If calcium is seen in the mitral valve, mitral stenosis, in this context, is virtually assured.

At catheterization, marked elevation of the pulmonary vascular resistance with a low cardiac output and critical reduction in calculated mitral valve area are the usual findings.

Silent mitral stenosis may simulate other diseases causing severe pulmonary hypertension such as chronic lung disease and recurrent pulmonary embolism. The history and physical findings may be indistinguishable. The electrocardiogram, roentgenographic and fluoroscopic findings will almost always be helpful in the differential diagnosis if one suspects silent mitral stenosis.

## Summary

Two cases of silent mitral stenosis have been presented. This entity, characterized by severe pulmonary hypertension, decreased cardiac output, and critical reduction in calculated mitral valve orifice size, should be suspected in the differential diagnosis of apparently unexplained pulmonary hypertension.

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(*Continued on page 605*)

# The Coronary Care Unit: Concept, Status and Needs

EDWARD B. CROSS, M.D., * AND J. EDGAR CASWELL, M.A.†

ONE OF THE MOST significant medical developments in recent years has been the rapidity with which specialized coronary care units for acute myocardial infarction patients have been established in many of the Nation's hospitals.

In the early 1960's the steadily increasing number of deaths resulting from coronary artery disease in the United States led, naturally enough, to a search for a means of effectively reducing the toll exacted by the major manifestation of this disease—myocardial infarction. The result was the development of a hospital intensive care area specifically designated to provide constant surveillance and emergency treatment of acute infarction patients.

The concept of such a facility was based on the premise that continuous monitoring of the patient's electrocardiogram and immediate application of cardiac resuscitation would result in a sizable decrease in the mortality experienced by hospitalized heart attack victims. Provided that early recognition and effective treatment take place, the greatest impact of the coronary care unit on mortality is realized through prompt and aggressive action which prevents the progression of rhythm disturbances to more severe forms and avoids circulatory complications.

The U. S. Public Health Service's Heart Disease Control Program has maintained a continuing interest in coronary care units from their conception to the Program's present primary interest in fostering the training of nursing personnel to staff these units.

The first 2 coronary care units were developed in 1962. One was opened in the spring of that year at Bethany Hospital in Kansas City, Kansas, through a grant from the John A. Hartford Foundation. The other was established in the fall at Presbyterian Hospital in Philadelphia, Pennsylvania, by means of a grant from the U. S. Department of Health, Education, and Welfare.

By 1965 more than 50 units were in operation. And today, less than 6 years since the opening of the first units, it is conservatively estimated that more than 350 hospitals have separate areas designed, equipped, and staffed to meet the total anticipated needs of the myocardial infarction patient. Another 250 hospitals contain general medical intensive care units that include electronic monitoring equipment for 1, 2, or 3 beds for infarction patients.

To date the Heart Disease Control Program has been instrumental in the development of 6 units. The principal interest of the Program in supporting these units has been to demonstrate their feasibility and value and to stimulate more basic research on this entire aspect of patient care.

When, at its outset, this entirely new concept attracted such a magnitude of interest throughout the country, the Heart Disease Control Program recognized the need for established guidelines to aid hospitals with the development of new units. The Public Health Service publication, "Coronary Care Units," was therefore prepared by the Program in 1964.[1] The initial printing was exhausted within a few months and the sixth edition is presently being published.

What are some of the elements that are generally considered essential for an effectively operating coronary care unit?

In the first place, the structure of the individual unit in any hospital will depend to a great extent upon the needs and capabilities of that hospital. For this reason it is neither entirely possible nor desirable to prescribe a rigid list of requirements that must be met in every respect before a unit is regarded as of optimum quality.

At the same time, the consensus of many directors of currently operating units indicates certain elements that should be provided for before establishment of a unit is considered. These include:

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1. Selection of a tranquil environment within the hospital for placement of the unit.
2. Provision of adequate space in the unit for proper patient surveillance and use of emergency equipment.
3. Establishment of a coronary care committee consisting of physician, nurse, administrator, and other personnel involved in the operation of the unit.
4. Organization of a cardiac arrest team to provide emergency care within the unit and throughout the hospital on a 24-hour basis.
5. Appointment of a physician-director and nurse-co-director of the unit.
6. Establishment of hospital policy regarding admission and transfer of patients to and from the unit.
7. Availability of a staff of nurses trained to properly staff the unit.

The last element in the above list is the most critical determinant of a unit's success. While, as has been noted, many aspects of a coronary care unit must depend upon the circumstances of the individual hospital, one aspect of unit operation appears to meet with universal agreement: The nurse in her function of carrying out the directions of the physician is one of the most vital elements of the unit.

At the 1965 Bethesda Conference of the American College of Cardiology on "Training Techniques for the Coronary Care Unit,"[2] the subcommittee on coronary care nursing made the following statement regarding the status of that field at that time:

"The role of the cardiac nurse specialist is of primary importance in the successful operation of the Coronary Care Unit.

"There is a clear need for specialized training of nursing personnel if the necessarily high level of competence in cardiac nursing is to be attained, with particular reference to an expanded role for the nurse in the utilization of cardiac monitoring equipment and in the performance of cardiopulmonary resuscitation.

"The present community need for qualified, trained nurses and training centers in coronary care is acute."

The need for nurses, "acute" in 1965, today has become considerably more critical.

Unfortunately, it is not uncommon today for a hospital to have available space and equipment for a coronary care unit but be unable to begin operation because of the lack of a staff trained in cardiovascular disease nursing.

A staff of 12 nurses specially trained in coronary care normally is required for a 5-bed unit. If each of the 1,200 200-bed hospitals in the United States established a 5-bed coronary care unit, training would be needed for more than 14,000 nurses.

Various methods have been used in attempts to prepare nurses for unit duty. Perhaps the most prevalent has been a period of short in-service education for nurses in hospitals that have units. Some hospitals have attempted to offer a short-term course, but often this has overburdened the hospital's staff and budget.

During recent months the Heart Disease Control Program has taken steps to help solve this serious problem. In July, 1966 the Program convened a group of experts in coronary care that included physician-directors, nurse-educators, and clinicians; together with the members of the Program they prepared a set of criteria and guidelines for nurse-training in coronary care units. Included are guidelines for the development of nurse-training centers, the selection of trainees, and the evaluation of the effectiveness of the training received.[3]

The Program recently has reviewed applications from some of the country's leading schools of nursing that are interested in receiving Program support for the creation of nurse-training centers. Selected schools are conducting special short-term courses in cardiovascular disease nursing.

It is hoped that an entire network of such training centers throughout the country offering instruction and refresher courses for coronary care unit personnel will someday be a reality. There can be little doubt that today this is a most urgent need for the continued development of coronary care units in the United States.

The coronary care unit has been widely accepted because of the demonstrated fact that the facility does have a great lifesaving capability. Despite its rapid development, however, the concept is relatively still in its infancy, and the determination of the ultimate extent of this capability awaits additional experience and investigation.

As an example, one of the most promising new developments is the recent interest in the introduction of computer systems into units that will, in effect, continually observe data from each patient (electrocardiogram, other vital signs, medications, etc.) and produce an integrated interpretation of patient status and prognosis. Such a system also will process and display data in order that the physician will be able to review patient status over the previous 8-hour period.

(*Continued on page 605*)

# The Role of a Comprehensive Intensive Care Unit in a General Hospital

MORRIS L. JAMPOL, M.D.,* ALBERT H. DOUGLAS, M.D.,† AND ERWIN LEAR, M.D.‡

In surveying current trends in hospital care during the past 5 years 2 developments have been apparent. The first is the widespread introduction of coronary care units for patients with myocardial infarction. The second is the concept of progressive patient care, namely, intensive care for the acutely ill patient and decreasing concentration of medical and nursing care as the patient convalesces. The role of the coronary care unit in saving lives during the first week of myocardial infarction has been substantiated in many centers.[1-6] The major complications of ischemic heart disease—arrhythmias, shock, and congestive failure—are always ominous. When these complications are anticipated, diagnosed promptly, and intensively treated the mortality may be greatly reduced.[7,8]

Physical designs for intensive care units, as well as equipment, personnel, and procedural routines, are now available, and many community hospitals have actively functioning intensive care coronary units.[9-12] These usually consist of a localized area of the hospital where a small number of beds (usually 4) are reserved for continuous monitoring after the onset of a myocardial infarction. Although equipment and emergency procedures have been standardized, the decisions as to which patient should be admitted to a coronary care unit and how long patients should be kept in the unit are still not easily made. It is extremely difficult to ascertain which patient will develop an arrhythmia or other serious complications. Most authors generally feel that the more patients monitored, the greater will be the saving of lives. This is especially true for the patient who has a cardiac arrest [12-15] in whom seconds and minutes spell the difference between life and death.

The chief limitation in the care of patients therefore has been the lack of adequate equipment and trained personnel. Yet coronary care beds may often go unutilized. If no appropriate patient is available, 1 or more beds may remain empty. As a matter of fact, some authorities recommend that 1 bed remain empty and available most of the time for an emergency admission. Thus, expensive equipment and highly trained personnel may be wasted as much as 25% of the time.

The intensive nursing skills as well as the medical sophistication needed for the care of the patient with myocardial infarction are too valuable to be underutilized. Furthermore, these facilities are equally applicable to other medical conditions, such as gastrointestinal hemorrhage, acute renal failure, the comatose patient, drug overdose, and fluid and electrolyte depletion. The physical equipment (including cardiac monitors, respirators, and other ancillary equipment) is just as vital for the noncoronary patient in shock or coma as it is for the coronary patient.[16] With a realization of these needs, the role of the Comprehensive Intensive Care Unit can be defined. This is an area in a general hospital which is the extreme end of the spectrum of hospital care, namely, the care of the sickest patients, including those with acute myocardial infarction. Our experience over a period of 2 years at the Queens Hospital Center in Jamaica, New York will be described.

The Queens Hospital Center in Jamaica, New York is a municipal hospital of 1,200 beds. The Intensive Care Unit as well as 90 per cent of the hospital beds is supervised through an affiliation contract with the Long Island Jewish Hospital. Thirteen medical beds are set aside in one area designated the Intensive Care Unit (figure 1). Mobile monitoring equipment is available for cardiac monitoring of 6 patients with myocardial infarction. Since patients with myocardial infarction are not necessarily confined to one area of the unit, the nursing supervisor may move beds and equipment about as necessary to make care more manageable. If 2 or 3 coronary occlusion patients arrive they are placed side by side and are easily in view of the nursing station. Two patients undergoing peritoneal dialysis may be side by side, and 1 nurse assigned to the fluid management can easily

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manage the 2 patients. Patients with infections can be isolated at one end of the unit, and cross infections can be minimized. Patients without myocardial infarction who need monitoring, i.e., those with pulmonary embolism, digitoxicity, and electrolyte abnormalities, can receive the same benefits as the patients with myocardial infarction.

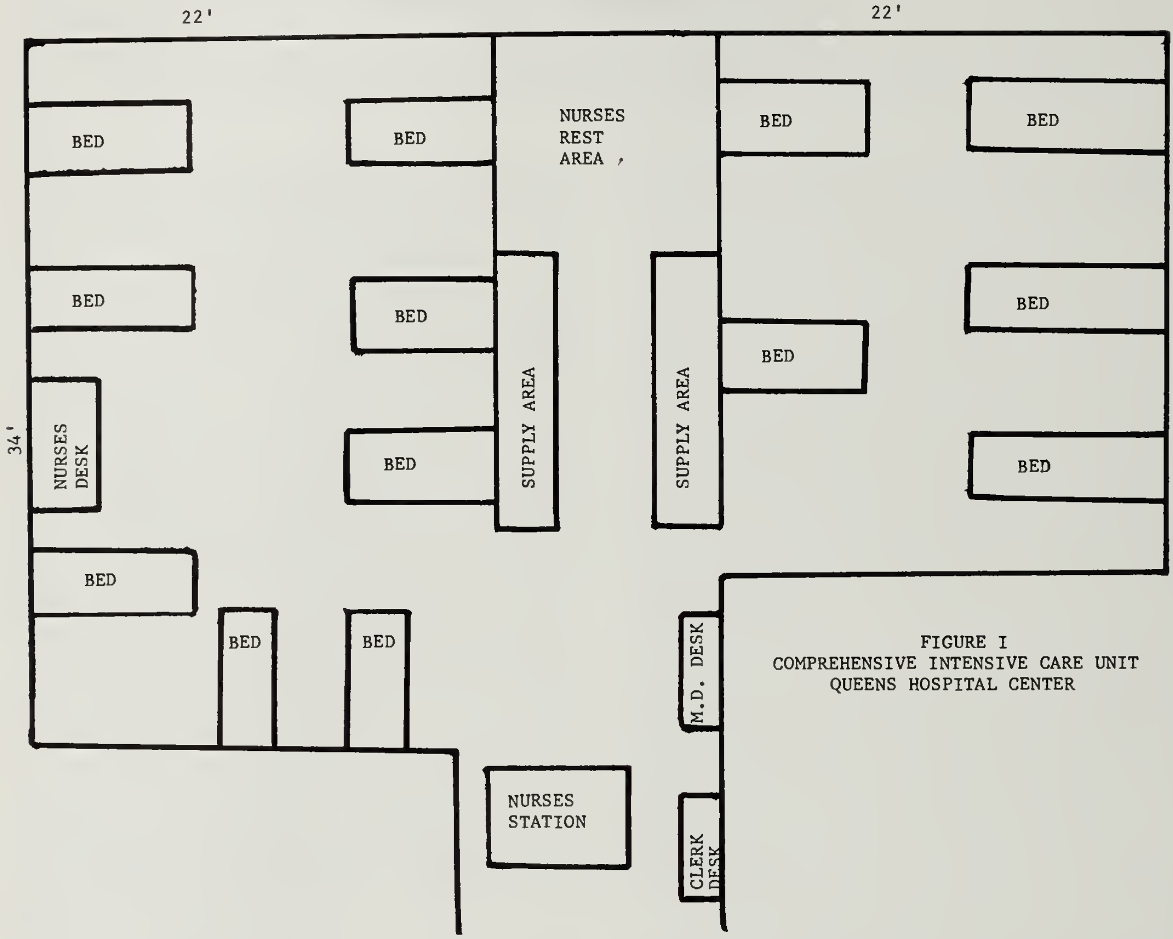

FIGURE I
COMPREHENSIVE INTENSIVE CARE UNIT
QUEENS HOSPITAL CENTER

What type of patients should be admitted to the Comprehensive Intensive Care Unit? Of course, patients with acute coronary occlusions are primary candidates. The presence of congestive heart failure, severe or prolonged pain, shock, and arrhythmias make cardiac monitoring imperative. However, ideally even the patient with apparently uneventful coronary occlusion will benefit from cardiac monitoring.[7,13] Patients with hemorrhage, shock, septicemia, convulsions, coma, or drug overdoses are routinely admitted. Other conditions such as diabetic acidosis, thyrotoxic crises, myxedema coma, Addisonian crises, malignant hypertension, and subarachnoid hemorrhage have all been treated. Our total experience for the first 2 years is listed in tables 1 and 2.

The equipment used is standard for coronary-care and intensive-care departments. Always available are cardiac monitors, pacemakers, cardioverters, defibrillators, and chest compressors. We make frequent use of ventilatory aids

**TABLE 1: Vital Statistics—Comprehensive Intensive Care Unit, Queens Hospital Center**
March 8, 1965 to February 28, 1967

| | | |
|---|---|---|
| Total No. Patients Admitted | | 997 |
| Disposition: | | |
| Deaths | 338 | |
| Transferred to ward | 613 | |
| Discharged home | 25 | |
| Signed out at own risk | 17 | |
| Remaining on Unit | 4 | |
| Length of Stay in Unit: | | |
| 1 day | 225 | |
| 2 days | 174 | |
| 3 days | 145 | |
| 4 days | 88 | |
| 5 days | 79 | |
| 6 days | 54 | |
| 7 days | 48 | |
| 8 days | 30 | |
| 9 days | 29 | |
| 10 days or more | 125 | |

**TABLE 2: Types of Cases Seen in Comprehensive Intensive Care Unit**
March 8, 1965 to February 28, 1967

| | |
|---|---|
| CARDIOVASCULAR DISEASE | |
| Myocardial infarction | 205 |
| Heart block | 58 |
| Aortic aneurysm | 4 |
| Pulmonary edema and congestive heart failure | 63 |
| Arrythmia | 12 |
| Malignant hypertension | 3 |
| Idiopathic heart disease | 2 |
| Shock, cause undetermined | 2 |
| Endocarditis, acute | 1 |
| Rheumatic fever | 1 |
| Digitalis toxicity | 1 |
| TOTAL | 352 |
| GASTROINTESTINAL DISEASE | |
| Hemorrhage | 157 |
| Pancreatitis, acute | 7 |
| Biliary disease | 3 |
| Postoperative carcinoma | 5 |
| Postoperative ulcer | 4 |
| Postoperative portocaval shunt | 1 |
| Postoperative hernia | 1 |
| Intestinal obstruction | 2 |
| Appendicitis | 2 |
| Mesenteric infarction | 1 |
| Peritonitis | 1 |
| TOTAL | 184 |
| RENAL DISEASE | |
| Chronic renal disease, uremia | 43 |
| Urinary retention | 1 |
| Acute glomerulonephritis | 1 |
| TOTAL | 45 |
| HEPATIC DISEASES | |
| Hepatic failure, coma | 12 |
| Cirrhosis; other | 2 |
| TOTAL | 14 |
| DIABETES MELLITUS | |
| Diabetic coma | 23 |
| Hyperosmolality coma | 1 |
| TOTAL | 24 |
| ALCOHOLISM, ACUTE | 2 |
| INFECTIOUS DISEASES | |
| Septicemia | 15 |
| Septic abortion | 2 |
| Salpingitis | 1 |
| Subphrenic abscess | 1 |
| Abscess of jaw | 1 |
| TOTAL | 20 |
| DRUG OVERDOSAGES | 94 |
| CENTRAL NERVOUS SYSTEM | |
| Subarachnoid hemorrhage | 39 |
| Cerebral thrombosis | 38 |
| Cerebral hemorrhage | 16 |
| Subdural hematoma | 15 |
| Meningitis | 12 |
| Cerebral concussion | 7 |
| Skull fracture | 5 |
| Epilepsy | 5 |
| Encephalitis | 3 |
| Delirium tremens | 3 |
| Brain tumor | 4 |
| Epidural hematoma | 1 |
| Guillain-Barré syndrome | 1 |
| Encephalomalacia | 1 |
| TOTAL | 150 |
| PULMONARY DISEASE | |
| Pulmonary infarction | 17 |
| Emphysema | 11 |
| Pneumonia | 10 |
| Status asthmaticus | 6 |
| Pneumothorax | 5 |
| Carcinoma of lung | 3 |
| Laryngospasm | 1 |
| Cor pulmonale | 1 |
| Pleural effusion | 1 |
| Stab wound of chest | 1 |
| TOTAL | 56 |
| HEMATOLOGIC DISEASE | |
| Purpura due to quinidine | 2 |
| Purpura, idiopathic | 1 |
| TOTAL | 3 |
| MISCELLANEOUS DISEASES | |
| Multiple fractures | 18 |
| Postaneurysm-resection | 6 |
| Metastatic carcinoma | 5 |
| Stevens-Johnson syndrome | 3 |
| Myxedema, coma | 2 |
| Thyroid storm | 2 |
| Postoperative splenectomy | 2 |
| Postoperative cholecystectomy | 2 |
| Multiple myeloma | 2 |
| Shock, cold exposure | 1 |
| Adrenal insufficiency | 1 |
| Viral illness | 1 |
| Severe burns | 1 |
| Postoperative thrombectomy | 1 |
| Muscular dystrophy | 1 |
| Lymphosarcoma | 1 |
| Incarcerated hernia | 1 |
| Anaphylactic shock | 1 |
| Heat stroke | 1 |
| Scleroderma | 1 |
| TOTAL | 53 |

including mechanical ventilators and intermittent positive-pressure apparatus. Endotracheal intubation by the Anesthesia Department and emergency tracheotomy by the Otolaryngology Department are readily available. Hypothermia blankets, gastric cooling, and central venous pressure monitoring are used when appropriate. Hemodialysis is available, although peritoneal dialysis is carried out more frequently.

The staff of the Comprehensive Care Unit is under the supervision of the Director of Medicine. It consists of a Visiting Physician-in-Charge (part-time) who directs the Unit's day-to-day activities. He makes rounds one or more times per day and is assisted by 2 Assistant Attending Physicians (1 part-time and the other full-time). These men are assigned from the General Medical Service for periods of 3 months. Thus, various junior members of the attending staff acquire intensive-care experience under the supervision of the Director and Physician-in-Charge. One assistant resident in medicine and 1 medical intern are assigned to the Unit for periods of 1 to 2 months. The house staff thus acquires direct experience in the care of the more acutely ill patients. An attending anesthesiologist and senior resident visit the Unit daily to supervise the management of the respiratory problems. The Unit therefore acts as a Respiratory Unit also. In addition, consultations are readily available from all of the medical subspecialties, including the Cardiology, Gastroenterology, Hematology, and Neurology Services. When indicated, close coöperation is maintained with the Surgical and Neurosurgical Departments.

The nursing care optimally consists of 1 registered nurse for each 2 patients. This, however, is not always realized, but assistance by practical nurses and student nurses is available. Lectures and indoctrination of nursing staff are continually carried out by the Physician-in-Charge. Training in the Comprehensive Intensive Care Unit is a highlight of the Nurses Training School.

Admission policy to the Unit is not too rigidly fixed. In general we try to accept any patient for whom the application of skilled medical nursing and mechanical equipment may bring about recovery. Terminal cases of irreversible disease are not accepted. However, if there is any doubt, patients are given a trial of care in the Unit. Decisions about patient admittance are made by the Physician-in-Charge, although in his absence, the Assistant Physicians, resident staff, or even the ICU charge nurse may accept a patient.

## Comment

The advantages of a Unit of this sort are many. The patient benefits from the use of the most modern techniques in diagnosis and management of acute illness. The available medical attendance as well as the intense nursing care often make the crucial differences in outcome. Arrhythmias are detected and treated promptly. Electrolyte problems can be managed effectively by an alert team. Bleeding patients can have hematocrits done at half-hour intervals, since these are performed by the intern on the Unit. Blood pH, $PCO_2$, and $PO_2$ can be carefully followed. Monitoring of vital signs in all patients as well as central venous pressure on selected patients is invaluable in good patient care. Cardiac massage, defibrillation, and pacing are available "on the spot," and precious time is not lost in alerting a resuscitation team.

The advantage to the hospital is manifold. Expensive equipment is not scattered in many areas but is concentrated in the Intensive Care Unit. Maximum utilization is thus obtained. Within the Unit itself the mobility of beds and equipment allows use of equipment for more patients. Fluids, medications, and usual and unusual drugs are stored in the ICU ready for instant use. This avoids emergency calls on the standard supply areas. The removal of the critically ill patients from the regular medical wards frees the house staff and nursing staff to take care of the more routine hospitalized patients, who are usually neglected if efforts on a ward are concentrated on 1 or 2 acutely ill patients.

The training features of our program have been most gratifying. Interns and residents rotate through the ICU and develop great confidence in handling acutely ill patients. Anesthesia residents develop proficiency in the management of respiratory problems. Nurses who have trained or worked in the Comprehensive Intensive Care Unit have acquired skills and experience which make their services more valuable on any ward. Finally, the concentration of equipment and staff makes the ICU an important place for controlled research and statistical evaluation of current methods of patient care.

Our thesis, therefore, is that the skills and equipment of a coronary care unit can be used sucessfully for other acute medical illnesses with equally rewarding results. Just as acute coronary care units save lives of patients with myocardial infarction, the Comprehensive Intensive Care Unit saves lives of patients with drug overdoses, acute renal failure, etc. Formerly these acutely ill patients would have special nurses who would give them individual personalized attention. However, special nurses, no matter how skillful or dedicated, cannot bring the newer knowledge and equipment to a desperately ill patient. By moving the patient into the Comprehensive Intensive Care Unit this knowledge will be applied by an experienced, readily available team of physicians and nurses.

## Summary

A Coronary Care Unit can easily be expanded into a Comprehensive Intensive Care Unit. We have detailed our first 2 years' experience with such a Unit. In addition to patients with myocardial infarction, the Unit receives patients with other acute conditions, such as gastrointestinal bleeding, shock, coma, drug overdosage, renal failure, etc. Equipment used in coronary care—monitors, pacers, defibrillators—are used advantageously on noncoronary as well as coronary patients. This makes concentrated medical and nursing care available for a wide variety of medical conditions. The benefits to the patient are unquestionable, but the bonus benefits in equipment utilization, staff-training, and hospital economy are equally rewarding. In the changing concept of progressive hospital care the Comprehensive Intensive Care Unit represents the extreme end of the spectrum and should be an integral part of a general hospital.

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### Silent Mitral Stenosis—Lenkin and Shugoll

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### Coronary Care Unit—Cross and Caswell

*(Continued from page 600)*

As new refinements and progress take place in this field the interest of the Heart Disease Control Program will remain that of implementing the optimum application of the coronary care unit in preventing the lethal complications of myocardial infarction.

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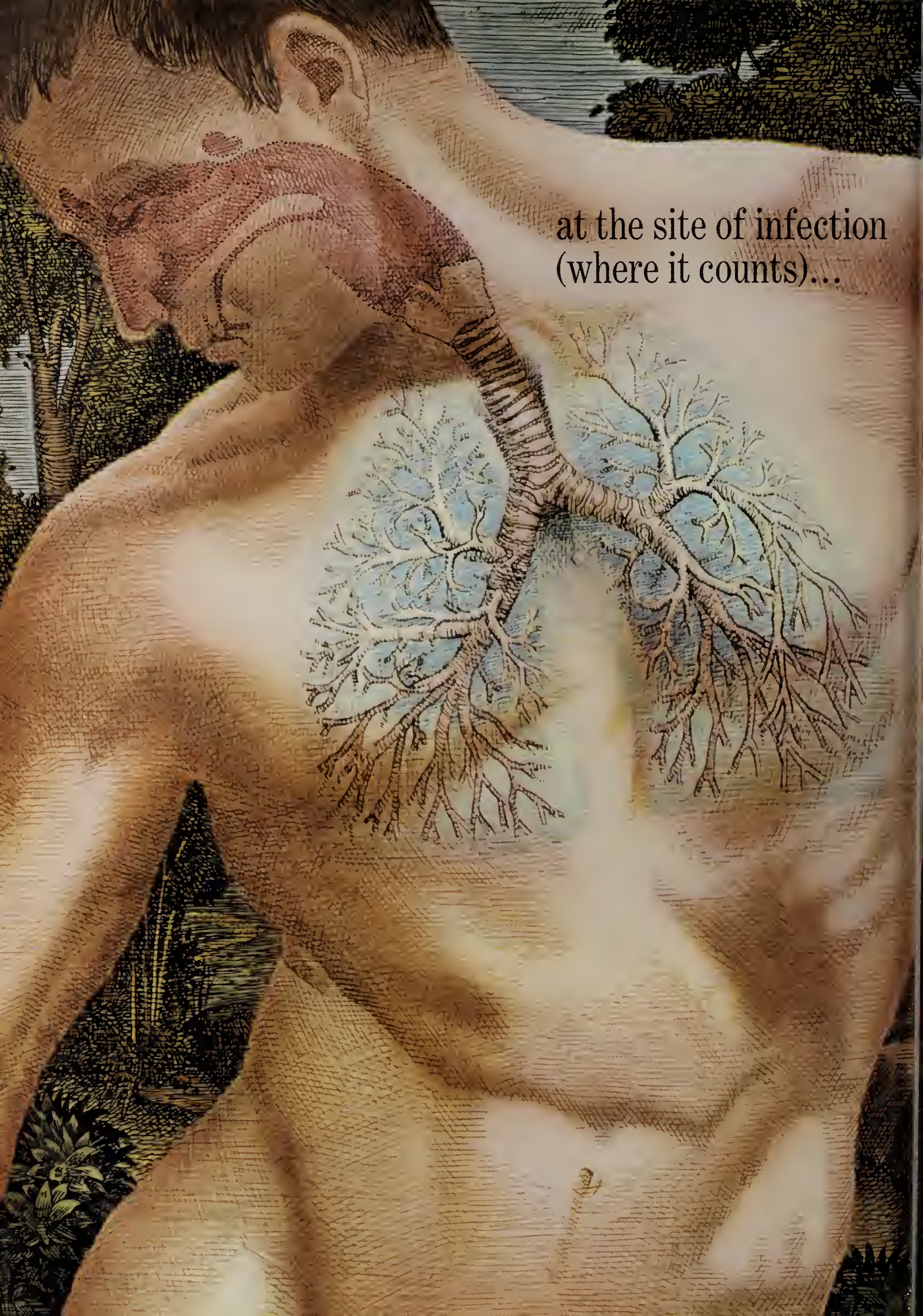
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In the treatment of acute bacterial pharyngitis and tonsillitis, this antibiotic has promptly eradicated the bacteria (streptococci) and has produced a parallel prompt clinical improvement. There have been no group A beta-hemolytic streptococci resistant to this preparation. In beta-hemolytic streptococcus infections, treatment should be maintained for ten days to prevent the development of rheumatic fever or glomerulonephritis.

Erythromycin estolate has proved to be very effective in pneumococcus pneumonia and in acute bronchitis with pneumococci on culture. Bronchopneumonia and otitis media in children have responded well to its use.

The antibiotic has been used very successfully in staphylococcus infections. Good therapeutic results have been obtained in soft-tissue infections, abscesses, cellulitis, carbuncles, wound infections, and furunculosis.

In serious staphylococcus infections, erythromycin preparations should be used only in combination therapy with other antimicrobial agents. As is the case with any treatment regimen used in these severe conditions, surgical procedures should be performed when indicated, and large dosages of the antimicrobial agents should be employed. In this fashion, Ilosone has been effective in staphylococcus pneumonia, osteomyelitis, septicemia, empyema, and meningitis.

Multiple 500-mg. doses of the drug have also been useful in gonorrhea and syphilis. Since penicillin is the drug of choice for the treatment of syphilis and gonorrhea, erythromycin estolate should be employed for these infections only in patients with a history of penicillin allergy. Also, other infections due to susceptible bacteria in patients known to be hypersensitive to penicillin or other antibiotics may be considered for treatment with Ilosone.

Contraindications: Ilosone is contraindicated in patients with a known history of sensitivity to this drug and in those with preexisting liver disease or dysfunction.

Adverse Reactions: Data obtained from seven years' use of propionyl erythromycin ester and erythromycin estolate (Ilosone) indicate that hepatic dysfunction with or without clinical jaundice may occur during or following courses of therapy with the drug.

Changes in liver function tests in such cases have been indicative of intrahepatic cholestasis. The symptoms appear to be the result of a form of sensitization. The initial symptoms have developed in some cases after a few days of treatment but generally have followed one or two weeks of continuous therapy or several courses of the drug. Symptoms reappear promptly, usually within forty-eight hours, if the drug is readministered to sensitive patients. Eosinophilia was noted in peripheral blood counts. The findings readily subsided without apparent residual effects when treatment was discontinued. Recovery was delayed in one reported instance. The physician indicated in this case that either drug-induced jaundice or viral hepatitis may have been responsible for the findings.

In one clinical study involving ninety-three patients treated with the antibiotic, three cases of jaundice were observed and an additional eleven cases developed some changes in liver function tests. Three of the patients had abnormal liver function tests a second time on readministration of the drug.

Even though it is assumed that not all cases of jaundice have been reported, it seems clear that the number is small compared with the amount of drug that has been used. Reported cases have included persons in whom there had been administered other drugs known to be associated at times with hepatic side-effects and cases in which the presence of viral hepatitis or other disease may have been responsible for the findings. In some of the cases, associated gastro-intestinal symptoms simulated the colic of biliary tract disease. In other instances, clinical symptoms and results of liver function tests resembled findings in extrahepatic obstructive jaundice. It appears that the occurrence of jaundice after administration of Ilosone is infrequent, but further investigations are being made to estimate its incidence more accurately.

In those cases mentioned above in which jaundice appeared to be definitely related to use of the drug, laboratory findings were characterized by increased direct-reacting bilirubin, elevated alkaline phosphatase levels, negative or weakly positive cephalin flocculation and thymol turbidity tests, elevated serum glutamic oxalacetic transaminase levels, peripheral eosinophilia, and normal cholecystograms.

Individual idiosyncrasy seems evident since jaundice has not been reported in other patients taking prolonged courses of the medication. Patients with chronic infection have been given 1 to 2 Gm. of the drug daily for periods of two to six months, and patients with rheumatic fever have taken prophylactic doses of 0.5 Gm. daily for two years without difficulty. In one group of 144 patients who received the drug daily for two years, no jaundice was noted. It was of interest that members of six of these patients' families, who were not taking the drug, had episodes of jaundice during the study period.

Transaminase and serum alkaline phosphatase levels were determined in a group of fifty-four adults and children who took 250 mg. of Ilosone daily for an average of sixteen months as rheumatic fever prophylaxis. The results were compared with those of a similar group of forty-four patients who received penicillin. There were no cases of jaundice in either group. Elevation of SGPT and serum alkaline phosphatase levels during the course of treatment was observed in one patient treated with Ilosone and in two patients treated with penicillin. Seven other patients in the group receiving Ilosone and four others in the penicillin group showed elevations in one of the tests at some time during administration of the drugs.

Very satisfactory therapeutic results, without toxicity, were reported in 102 pediatric patients who received short-term (ten-day) courses of Ilosone in the treatment of streptococcus infections. Results of liver function tests in these patients were comparable to those in a similar control group who had received penicillin.

Gastro-intestinal disturbances not associated with hepatic effects are observed in a small proportion of individuals as a result of a local stimulating effect of the medication on the alimentary tract; however, the normal intestinal gram-negative bacterial flora is not appreciably altered by erythromycin drugs.

Although allergic manifestations are uncommon with the use of erythromycin, there have been occasional reports of urticaria, skin eruptions, and, on rare occasions, anaphylaxis.

Administration and Dosage: Ilosone is administered orally.

Ilosone Pulvules®, Ilosone Liquid 125, Ilosone, 125, for Oral Suspension, Ilosone Drops, Ilosone Chewable Tablets.

For infants and for children under twenty-five pounds of body weight, the usual dosage is 5 mg. per pound every six hours; for children twenty-five to fifty pounds, 125 mg. every six hours. (Tablets Ilosone Chewable should be chewed or crushed and swallowed with water.)

For adults and for children over fifty pounds, the usual dosage of Ilosone is 250 mg. every six hours.

For severe infections, these dosages may be doubled.

When larger doses are indicated, parenteral erythromycin therapy should be considered.

In the treatment of syphilis, the recommended total dosage is 20 to 30 Gm. given in divided doses for a period of ten to fifteen days. Close follow-up of the patient is necessary since erythromycin drugs have not had adequate evaluation in all stages of syphilis. Examinations of spinal fluid are recommended as part of the follow-up therapy.

For gonorrhea, 500 mg. four times a day for four days are recommended. In the treatment of gonorrhea, patients with a suspected lesion of syphilis should have a dark-field examination before receiving antibiotics, and monthly serologic tests should be made for a period of three months.

How Supplied: Pulvules Ilosone, Capsules, N.F., 125 and 250 mg. (equivalent to base), in bottles of 24 and 100.

Ilosone Liquid 125, Oral Suspension, U.S.P., 125 mg. (equivalent to base) per 5-cc. teaspoonful, in 60-cc. and pint-size packages.

Ilosone, 125, for Oral Suspension, N.F., 125 mg. (equivalent to base) per 5-cc. teaspoonful, in 60 and 150-cc.-size packages.

Ilosone Drops, 5 mg. (equivalent to base) per drop, in 10-cc.-size packages, with dropper calibrated at 25 and 50 mg.

Tablets Ilosone Chewable, N.F., 125 mg. (equivalent to base), in bottles of 50. [032767]

*References:* 1. Griffith, R. S., and Black, H. R.: Am. J. M. Sc., *247*:69, 1964.
2. Griffith, R. S., and Black, H. R.: Antibiotics & Chemother., *12*:398, 1962.
3. Hirsch, H. A., Pryles, C. V., and Finland, M.: Am. J. M. Sc., *239*:198, 1960.

*Additional information available to physicians upon request.*
*Eli Lilly and Company, Indianapolis, Indiana 46206.*

Lilly

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# PRESIDENT'S PAGE

## THE 1967 SCIENTIFIC ASSEMBLY— A COMMEMORATIVE EVENT

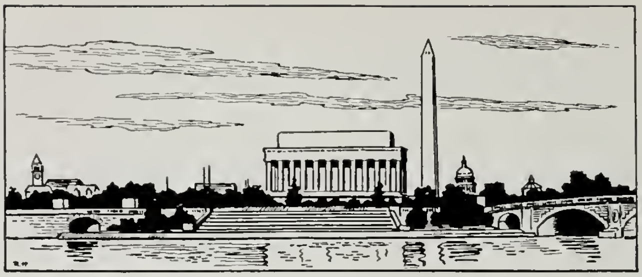
The Scientific Assembly of the Medical Society of the District of Columbia to be held this year will be surrounded with a special aura of significance, because this is the 150th anniversary of the founding of our organization. How many of us are really aware of the tremendous advances in the science of medicine which have occurred since the birth of our Society? Our Assembly is a vibrant expression of a continuing effort to provide our members, as well as all of the medical profession within reach, with up-to-date reviews and analyses of procedures and techniques—evaluation of the old and introduction to the new.

The practice of medicine has become so complex, diversified, and specialized that your Committee on Arrangements, ably led by Dr. James A. Curtin, has perforce abandoned any attempt to cover all areas; instead he has selected relatively few topics of broad range and universal interest in order to present a thorough and concentrated educational exercise which, we hope, will prove of value to the majority of those who attend.

We hope that the meeting this year will be judged a fitting commemoration of our sesquicentennial. We hope that our 150-year longevity will not give evidence of senility but rather of wisdom and good judgment, learning and experience, to be applied with increasing skill in the years to come, thus providing the very best in medical care to the total community. Let us all make this occasion an opportunity to rededicate ourselves to the unchanging basic principles which form the foundation of medical practice and strive to serve with greater credit and benefit.

I am proud to be your 100th President during this Anniversary Year. I wish all of you both pleasure and profit as a result of this Assembly.

Henry D. Ecker



# EDITORIALS

## Participation—One Road to Learning

The Program for the Annual Scientific Assembly for 1967 will once again focus on certain topics or a theme in preference to unrelated papers. This will permit any physician in the Washington Metropolitan Area to attend meetings on those days or portions of days which reflect his interests. The subjects encompass many of the specialties as well as general medicine. The discussants are well qualified to present not only the practical aspects of patient management but also to bring us up to date on the mechanistic aspects of disease.

The continuing education of the physician is a popular topic but not a new one. Despite all the talk and writing, in medicine as well as in mathematics, "There is no royal road . . . . "

There is no single best method for education. According to past experience the audience at this Assembly will be composed of physicians who attend their hospital conferences, their specialty programs, and other courses in postgraduate medicine. We welcome them, of course. We think the responsibility of the Medical Society, however, extends in a special way to those physicians who have not developed the habit of attending medical meetings. We ask, in particular, that these physicians review this program and arrange their schedule so that they may participate.

James A. Curtin, M.D.
*General Chairman, 1967 Scientific Assembly*

## The Sixth Annual Davidson Lecture

Dr. Leslie H. Farber, well known psychiatrist and psychoanalyst, will be the guest lecturer at the Sixth Annual Davidson Lecture on Religion and Medicine, October 24, 1967, at 8:15 p.m. in the Exhibit Hall of the Medical Society Building. The heart of Dr. Farber's contribution to contemporary psychological thought is his insight into the human faculty of will, described by essays in his book, "The Ways of the Will."

Dr. Farber is a training analyst for the Washington Psychoanalytic Institute and consultant to the National Institute of Mental Health and Walter Reed General Hospital. Presently Chairman of the Association of Existential Psychology and Psychiatry of New York, Dr. Farber is a diplomate of the American Board of Psychiatry and Neurology in psychiatry and a Fellow of the American Psychiatric Association and the American College of Physicians. He formerly served as chairman of the faculty of the Washington School of Psychiatry and as Vice President of the William Alanson White Psychiatric Foundation.

Dr. Farber has chosen as his topic for discussion, "The Willfulness of Modern Existence." Generating the discussion period following Dr. Farber's lecture will be Rabbi Norman Gerstenfeld of the Washington Hebrew Congregation, representing the clergy, and Dr. Charles Waters Thompson, representing the medical profession.

As most of the Annals' readers know, the Davidson Lecture is a befitting memorial to Dr. E. Y. Davidson, whose initiation and guidance were responsible for the successful erection of the Society's first "home" at 1718 M Street, N.W. The Davidson Lecture was formerly presented by the physician who submitted, in competition, the most outstanding paper on medical research. Then in 1961 the Committee on Liaison with the Clergy of the Medical Society, realizing the growing need for establishing a close bond between clergymen and physicians, requested that a Lecture Series be developed to stimulate this program.

## Community Health Week

### October 15–21, 1967

The Medical Society of the District of Columbia will again participate in the annual observance of Community Health Week. This national AMA-sponsored program is designed to catch the public's eye and ear as we all "team up for better health."

We as physicians are the fulcrum of the health team—the third largest industry in the United States. Community Health Week presents a unique opportunity for physicians to demonstrate that they are the leaders of the team entrusted with the health of the public.

Screening tests for vision, glaucoma, chest X-rays, hearing, blood and blood-typing will be offered to everyone in the Washington Metropolitan Area at the Medical Society Building and at the District of Columbia General Hospital. Abnormal findings will be reported to the patient and to his physician. In addition, members of the Society and its Speakers Bureau will discuss various health problems on radio and television. Every member of the Society is reminded that he too is part of the Health Team and is urged to participate in public service programs during Community Health Week. We as physicians have much to offer the public, our patients, and the allied health fields when we exert true leadership in community health projects.

Warren D. Brill, M.D.
*Chairman, Committee on Public Information and Education*

## Current Recommendations for Influenza Immunization

The Surgeon General of the Public Health Service has been advised by his Committee on Immunization Practices that there most likely will be an increase in the number of cases of $A_2$ influenza during the 1967–1968 season, especially in the eastern part of the country, over that which occurred in 1966–67.

The National Communicable Disease Center has, therefore, recommended for use this season the newly introduced bivalent vaccine for preventive immunization. This vaccine contains only contemporary $A_2$ and B strains and will provide greater protection against current strains of influenza. The traditional polyvalent vaccine containing older strains (types A and $A_1$) as well as new $A_2$ and B antigens (in order to stimulate a broader immunologic response) will be available. However, the older strains, it is thought, will not play a significant role against the currently prevalent viruses. Both vaccines, the bivalent and polyvalent formulations, contain the same total quantity of influenza antigens—600 chick cell agglutinating (CCA) units. This limit is set in order to minimize the frequency of local and systemic reactions. Consequently, the new bivalent vaccine contains a greater proportion of $A_2$ and B strains than is possible in the polyvalent vaccine which retains A and $A_1$ antigens. Because of this the bivalent vaccine should provide greater protection against current strains of influenza than has previously been possible.

The Medical Society's Committee on Communicable Diseases recommends the bivalent vaccine for immunization for influenza this season. Its usage remains the same as heretofore. Persons who may require immunization and have not been vaccinated since July 1963 should receive an initial subcutaneous dose as soon as practicable after October 1, 1967 and a second, 2 months later. Ideally, the series of 2 doses should be completed by early December 1967. There is a 2-week interval between vaccination and development of antibodies. Only a single booster of bivalent vaccine at the dosage level specified for the primary series is necessary for individuals requiring immunization who have been vaccinated as recently as July 1963. The vaccine is contraindicated for anyone who is hypersensitive to eggs or egg products. Children under 10 years of age may have a febrile reaction following introduction of the vaccine, which may be treated with an antipyretic.

John R. Pate, M.D.
*Chairman, Committee on Communicable Diseases*

## Cleaner Air Week—October 22–28

Despite the absence of heavy industry, the Washington Metropolitan Area has a serious air pollution problem:

We have 4,100 cars per square mile, compared with Los Angeles' 1,350, Philadelphia's 3,730, and New York's 2,200. This is the source of the most worrisome pollutant—unburned gasoline.

Gasoline consumption in the D. C. area pours 2,000 tons of carbon monoxide, 224 tons of hydrocarbons, and 77 tons of nitrogen oxides into the air every day.

In our community we burn 2,400 tons of trash and unmeasured quantities of construction refuse and leaves every day.

In an average day we burn 6,000 tons of coal, 200 million cubic feet of gas, and over 1 million gallons of fuel oil.

The D. C. Public Health Service has detected photochemical smog at concentrations which produce eye irritation, vegetation damage, and visibility reduction on about 30 days each year. At times sulfur dioxide has combined with moisture in the air to form acid and even dissolved stockings on pedestrians.

"Exposure to relatively low levels of urban air pollution over months to years predisposes people —even those who don't smoke—to chronic bronchitis, emphysema, lung cancer, pneumonia and chronic heart disease. . . .

". . . There is a threat that a combination of weather conditions will allow the pollutants to stagnate and become highly toxic so that this city may experience an acute epidemic of smog poisoning with fatalities such as have occurred in other cities. . . ."[1]

Greater Washington Citizens for Clean Air has been organized to fight this problem by:

Educating the public on the problem of local air pollution. Concentrated efforts toward this objective will be made during Cleaner Air Week, October 22–28.

Encouraging citizen support of official agencies and legislation to curb air pollution.

Promoting the coördination of clean-air activities among the District of Columbia, Maryland, Virginia, Federal and regional agencies.

Encouraging total city planning which considers air pollution an environmental factor of serious concern for urban America.

Stimulating research and utilization of developments in:

—The effects of air pollution on human health.

—More effective and economical ways of reducing pollution from the employment of existing fuels.

—New pollution-free energy sources.

—Pollution-free methods of disposing of solid wastes.

Physicians interested in this problem are invited to become members of GWCCA. Individual membership is $5 per year. Application should be made to Miss Connie Foley, Secretary-Treasurer, 1714 Massachusetts Avenue, N.W., Washington, D. C. 20036.

Join Greater Washington Citizens for Clean Air in this fight!

Patrick J. Doyle, M.D.

Editor's note: Dr. Doyle is Chairman of the Department of Community Medicine and International Health at Georgetown University School of Medicine; a member of the Committee on Rehabilitation and Chronic Illness of the D.C. Medical Society; and a Board member of Greater Washington Citizens for Clean Air.

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[1] Policy Statement of The Medical Society of the District of Columbia on air pollution, August 1966.

## Any Physician-Poets in Washington?

The next Annual Book Number of J.A.M.A. (which is scheduled to appear in April 1968) will give some prominence to poetry written by physicians. In an editorial in the August 28 issue of J.A.M.A., an invitation is extended "to all physicians who write serious poetry to submit their works to this journal for consideration. We welcome all contributions, and those that are of sufficiently high quality we propose to print in our 1968 Book Issue. Physician-poets may write on any subject that they please. And lest we be accused of discrimination, we might say that we would also consider poetry written by nonphysicians, provided the verse has a medical subject matter or medical relevance."

Washington physicians have made for themselves a fine reputation in the creative arts through music and painting. If to some the gift of poetry has also been granted now is the time to bring it out of hiding.

# OFFICIAL PROGRAM

## *1967 Scientific Assembly*
## *The Medical Society of the District of Columbia*

## STATLER HILTON HOTEL

## *Scientific Program*

### MONDAY MORNING, NOVEMBER 20, 1967

(All Meetings in the Presidential Ballroom)

**James A. Curtin, M.D.,** *Presiding*
General Chairman, 1967 Scientific Assembly

**9:25** Welcome by **Henry D. Ecker, M.D.,** President, The Medical Society of the District of Columbia

### PANEL ON MEDICAL PROBLEMS INVOLVING THE TEENAGER

Moderator: **Felix P. Heald, M.D.**

Chief, Adolescent Medicine, Children's Hospital of the District of Columbia; Chairman, Department of Pediatrics, George Washington University School of Medicine

**9:30** **ADOLESCENT MEDICINE: FACT OR FALLACY?**
**Felix P. Heald, M.D.**

**9:45** **DRUG USAGE AND THE LAW: THE ADOLESCENT AND AN ARCHAIC CONCEPT**
**William Barton, M.D.**
Attending Physician in Psychiatry and Consultant to Adolescent Medicine, Children's Hospital of the District of Columbia

**10:00** **MENSTRUATION IN THE ADOLESCENT GIRL AND DEVIATIONS FROM THE NORMAL**
**Mary Z. Daugela, M.D.**
Faculty Associate, Adolescent Unit, Children's Hospital of the District of Columbia; Clinical Assistant Professor of Pediatrics, Georgetown University School of Medicine

**10:15** Recess to Visit Exhibits

**10:30** **SURGICAL PROBLEMS OF THE ADOLESCENT**
**Judson Graves Randolph, M.D.**
Surgeon-in-Chief, Children's Hospital of the District of Columbia; Associate Professor of Surgery, George Washington University School of Medicine

**10:45** **GROWTH PROBLEMS IN ADOLESCENCE**
**C. Andrew Rigg, M.D.**
Assistant Chief, Adolescent Unit, Children's Hospital of D. C.

**11:00** **THE EFFECT OF THE PUBERTAL GROWTH SPURT ON CONGENITAL HEART DISEASE**
**Lewis P. Scott III, M.D.**
Chief, Cardiology Section, Children's Hospital of D. C.

**11:15** Questions and Answers

**12:00** Recess for Lunch—Visit Exhibits

## MONDAY AFTERNOON, NOVEMBER 20

**Frank S. Bacon, M.D.,** *Presiding*

First Vice President, The Medical Society of the District of Columbia

### 2:00 PANEL ON MECHANISM OF DRUG-INDUCED DISEASE

MODERATOR: **Hyman J. Zimmerman, M.D.**

Chief, Liver and Metabolic Research Laboratory, Veterans Administration Hospital, Washington; Professor of Medicine, George Washington University School of Medicine

EPIDEMIOLOGIC ASPECTS OF ADVERSE REACTIONS TO DRUGS
**Leighton E. Cluff, M.D.**
Professor and Chairman, Department of Medicine, University of Florida School of Medicine

TYPES OF DRUG-INDUCED DISEASE
**Louis Lasagna, M.D.**
Associate Professor of Medicine and of Pharmacology and Experimental Therapeutics, Johns Hopkins University School of Medicine

MECHANISMS OF DRUG TOXICITY
**Bernard B. Brodie, M.D.**
Chief, Laboratory of Chemical Pharmacology, National Heart Institute, National Institutes of Health, Public Health Service, U. S. Department of Health, Education, and Welfare

DRUG-INDUCED HEPATIC INJURY
**Howard E. Ticktin, M.D.**
Associate Professor of Medicine, George Washington University School of Medicine; Chief of Service, George Washington Medical Division, D. C. General Hospital

## MONDAY, NOVEMBER 20, 8:00 P.M.

**Henry D. Ecker, M.D.,** *Presiding*

President, The Medical Society of the District of Columbia

### PUBLIC MEETING: DON'T BREATHE THE AIR

MODERATOR: **Sol Katz, M.D.**

Chief, Medical Service, Veterans Administration Hospital, Washington; Professor of Medicine, Georgetown University School of Medicine

INTRODUCTORY REMARKS
**The Honorable Gilbert Gude**
Congressman, Eighth District of Maryland

DEFINITION OF THE PROBLEM
**James H. Sterner, M.D.**
Medical Director, Eastman Kodak Company

WHERE ARE WE HEADING?
**Richard A. Prindle, M.D., M.P.H.**
Assistant Surgeon General (PHS); Director, Bureau of Disease Prevention and Environmental Control, Public Health Service, U. S. Department of Health, Education, and Welfare

WHAT SHALL WE DO?
**The Honorable Austin N. Heller**
Commissioner, New York City Department of Air Pollution Control

SUMMARY AND CLOSING REMARKS

## TUESDAY MORNING, NOVEMBER 21

**Margaret M. Kenrick, M.D.**, *Presiding*

Second Vice President, The Medical Society of the District of Columbia

### MODERN MEDICINE—DIAGNOSIS AND THERAPY

9:30 **BEE STING ALLERGY**

**Halla Brown, M.D.**

Professor of Medicine, George Washington University School of Medicine

10:10 Recess to Visit Exhibits

10:30 **OPHTHALMOLOGIC MANIFESTATIONS OF SYSTEMIC DISEASE**

**Irving H. Leopold, M.D.**

Chairman and Professor, Department of Ophthalmology, Mount Sinai School of Medicine, New York

11:10 **CURRENT STATUS OF MYOCARDIAL REVASCULARIZATION**

**Donald B. Effler, M.D.**

Chief, Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic Foundation, Cleveland, Ohio

(Dr. Effler's participation is made possible through the courtesy of the Washington Heart Association.)

11:50 Questions and Answers

12:00 Recess for Lunch—Visit Exhibits

## TUESDAY AFTERNOON, NOVEMBER 21

**Karl C. Corley, M.D.**, *Presiding*

Chairman, Executive Board, The Medical Society of the District of Columbia

### PANEL ON LOW BACK PAIN

Moderator: **William E. Reefe, M.D.**

Chief, Rheumatology Section, Veterans Administration Hospital, Washington; Assistant Professor of Medicine, Howard University College of Medicine

2:00 **DIFFERENTIAL DIAGNOSIS OF LOW BACK PAIN**

**William E. Reefe, M.D.**

2:35 **EXAMINATION OF THE PAINFUL LOW BACK**

**G. W. Hyatt, M.D.**

Professor of Surgery (Orthopedics), Georgetown University School of Medicine

3:00 Recess to Visit Exhibits

3:20 **CONSERVATIVE TREATMENT OF LOW BACK PAIN**

**Hans Kraus, M.D.**

Associate Professor of Physical Medicine and Rehabilitation, New York University School of Medicine

3:45 **PSYCHIATRIC ASPECTS OF LOW BACK PAIN**

**John C. Nemiah, M.D.**

Psychiatrist, Massachusetts General Hospital, Boston; Assistant Professor of Psychiatry, Harvard Medical School

4:10 Questions and Answers

**PROGRAM APPROVED BY AAGP**

This Assembly's Scientific Program has been approved by the American Academy of General Practice for its members for a maximum of 15 hours' credit under Category I.

## WEDNESDAY MORNING, NOVEMBER 22

**William S. McCune, M.D.,** *Presiding*

President-elect, The Medical Society of the District of Columbia

### PANEL ON PSYCHOSOMATIC MEDICINE: PROBLEMS OF CONSULTATION AND COLLABORATION BETWEEN PSYCHIATRY AND OTHER MEDICAL DISCIPLINES

9:30 THE NONPSYCHIATRIST PHYSICIAN AND THE PSYCHIATRIST CONSULTANT

**Philip Solomon, M.D.**

Physician-in-Chief, Psychiatry Service, Boston City Hospital; Associate Clinical Professor of Psychiatry, Harvard Medical School

9:50 EXPERIENCES IN MEDICAL PSYCHIATRIC LIAISON IN A GENERAL HOSPITAL

**David R. Hawkins, M.D.**

Professor and Chairman, Department of Psychiatry, University of Virginia School of Medicine, Charlottesville

10:10 PSYCHOSOMATIC DISORDERS OF CHILDHOOD

**Julius B. Richmond, M.D.**

Dean of the Medical Faculty and Chairman, Department of Pediatrics, State University of New York Upstate Medical Center, Syracuse

10:30 PROBLEMS OF PSYCHIATRIC CONSULTATION IN A GENERAL HOSPITAL

**William A. Greene, M.D.**

Professor of Medicine and Psychiatry, University of Rochester School of Medicine and Dentistry

10:50 Discussion—Questions and Answers

# *The Scientific Exhibit*

All Exhibits Open Monday and Tuesday, 9 A.M. to 5 P.M.;
Wednesday, 9 A.M. to 2 P.M.

As the Annals goes to press the following exhibits and exhibitors have been assigned space.

**"POOR MAN'S AUTOMATION" IN THE LABORATORY**

Richard E. Kelso, M.D., Washington

**SILICONE IN PLASTIC SURGERY**

J. Gordon Bell, M.D., Chief of Plastic Surgery, Doctors Hospital

**I.U.C.D.—ADVANCES IN 1967**

Robert J. Sherman, M.D., Washington

**THE USE OF A COVERED SUTURE TECHNIQUE FOR THE PLACEMENT OF AORTIC AND MITRAL VALVULAR PROSTHESES**

Charles A. Hufnagel, M.D., Department of Surgery, Georgetown University Medical Center

**TRANSVENOUS CARDIAC PACING**

Nicholas P.D. Smyth, M.D., Chairman, Department of Surgery, and James M. Bacos, M.D., Department of Medicine, Washington Hospital Center

**EXPERIMENTAL PEPTIC ULCER**

Paul E. Shorb, Jr., M.D., and Jerome W. Canter, M.D., Department of Surgery, George Washington University School of Medicine

**ALLERGY INFORMATION BOOTH**

D. C. Allergy Society

**LESIONS OF THE PALATE**

Colonel William G. Sprague, USAF, DC, Chief, Dental and Oral Pathology Division, and

Major James K. Jacoby, USAF, DC, Armed Forces Institute of Pathology

**STOP ORAL CANCER**

William L. Ross, M.D., Chief, Cancer Control Program, Public Health Service, Department of Health, Education, and Welfare

**SARCOMAS OF THE UTERUS**

Herbert B. Taylor, M.D., Lt. Comdr. Luther A. Youngs III, MC, USN, and Henry J. Norris, M.D., Armed Forces Institute of Pathology

**DEEP PALPATION REVEALS RENAL ANOMALIES IN THE NEWBORN**

Comdr. Melvin Museles, MC, USN, Chief of Pediatrics, United States Naval Hospital

**CONJOINED TWINS—OBSTETRICAL AND SURGICAL PROBLEMS**

George B. Callahan, M.D., Waukegan, Ill.; Victory Memorial Hospital and St. Therese Hospital, Waukegan, Ill.; Women's Hospital, Bangkok, Thailand; and International Associates

**SAFETY STANDARDS FOR FEDERALLY-OWNED VEHICLES**

Injury Control Program of the National Center for Urban and Industrial Health, Bureau of Disease Prevention and Environmental Control, Public Health Service, Department of Health, Education, and Welfare

**A PHONE CALL AWAY—AN EMERGENCY PSYCHIATRIC CONSULTATION SERVICE**

Department of Public Health, Government of the District of Columbia

**THE AIR WE BREATHE**

D.C. Department of Public Health

**PROCTOSIGMOIDOSCOPY FOR ASYMPTOMATIC CANCER**

American Cancer Society, District of Columbia Division, Inc.

Also exhibiting will be the D. C. Association of Medical Assistants, District of Columbia Political Action Committee (DOCPAC), and Medical Service of the District of Columbia.

# *The Technical Exhibit*

All Exhibits Open Monday and Tuesday, 9 A.M. to 5 P.M.;
Wednesday, 9 A.M. to 2 P.M.

As the Annals goes to press the following companies have contracted for space in the Technical Exhibit. The Assembly is made possible through the financial assistance of these Exhibitors. They have something of interest to display and a visit to each and every booth is suggested.

**ABBOTT LABORATORIES**
North Chicago, Illinois

**ALAN G. DAY**
Baltimore, Maryland

**ALOE MEDICAL**
St. Louis, Missouri

**AMERICANA CORPORATION**
Beverly Hills, California

**ARCUM PHARMACEUTICAL CORPORATION**
Vienna, Virginia

**AYERST LABORATORIES**
New York, New York

**BARRINGTON RESEARCH ASSOCIATES**
Cranbury, New Jersey

**BEECHAM RESEARCH LABORATORIES, INC.**
New York, New York

**BETHMNOT SURGICAL SUPPLY COMPANY**
Bethesda, Maryland

**BEUCHLER'S**
Washington, D. C.

**BOYCE AND LEWIS, INC.**
Washington, D. C.

**BREON LABORATORIES, INC.**
New York, New York

**BRISTOL LABORATORIES**
Syracuse, New York

**BURROUGHS WELCOME & CO., INC.**
Tuckahoe, New York

**BURTON, PARSONS & COMPANY, INC.**
Washington, D. C.

**CAPITAL HOSPITAL SUPPLY CORP.**
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# *Social Events*

## GEORGE WASHINGTON UNIVERSITY MEDICAL ALUMNI LUNCHEON

Monday, November 20, 1967—12:00 Noon—South American Room
Guest Speaker: **Harry F. Dowling, M.D.**
Professor and Head, Department of Medicine, University of Illinois College of Medicine
Tickets ($5.50) available at Medical Alumni Office or at Assembly Registration Desk.

## WOMAN'S AUXILIARY LUNCHEON

Monday, November 20, 1967—12:00 Noon—Gallery Room
Guest Speaker: **Representative Margaret Heckler** (R.) Massachusetts
Tickets ($6.00) available at Advance Registration* or Assembly Registration Desk.

## ANNUAL MEDICAL SOCIETY LUNCHEON

Tuesday, November 21, 1967—12:15 p.m.—Presidential Ballroom
Guest Speaker: **Charles L. Hudson, M.D.**
Immediate Past President, American Medical Association
Free tickets (for 300 members) available at Advance Registration or Assembly Registration Desk.

## DOCTORS' OFFICE STAFF DINNER

Tuesday, November 21, 1967—7:30 p.m.—Presidential Ballroom
Entertainment by Singing Air Force Sergeants
Tickets ($9.50) available at Advance Registration or Assembly Registration Desk.
Cocktails (6:30 p.m.) courtesy of Russell, Marsh & Kennedy

## GEORGETOWN UNIVERSITY MEDICAL ALUMNI LUNCHEON

Wednesday, November 22, 1967—12:00 Noon—South American Room
Guest Speaker: **The Reverend Edward B. Bunn, S.J.**
Chancellor and Past President (1952–1964) of Georgetown University
Father Bunn, a member of the Jesuit Order for 50 years, will be the guest of honor.
Tickets ($5.00) available from Dr. Raymond A. Osbourn or at Assembly Registration Desk.

## UNIVERSITY OF MARYLAND MEDICAL ALUMNI LUNCHEON

Wednesday, November 22, 1967—12:15 p.m.—Pan American Room
Guest Speaker: To be announced
Tickets available at Medical Alumni Office or at Assembly Registration Desk.

## ANNUAL RECEPTION AND DINNER DANCE

Wednesday evening, November 22, 1967
Presidential Ballroom
Cocktails at 6:30 p.m.—Dinner at 8:00 p.m.
Dancing at 9:00 p.m.—Music by Meyer Davis
Tickets ($11.50 per person) available at Advance Registration or Assembly Registration Desk.
Cocktail Party—Courtesy of Peoples Drug Stores
Music—Courtesy of Burton, Parsons & Company, Inc.
For this traditionally enjoyable affair, we are most indebted to both organizations.

---

*Advance Registration will be held at the Medical Society's Offices, November 17 and 18, from 8:30 a.m. to 4:45 p.m.

# Diagnosis:

## cystitis?
## pyelonephritis?
## pyelitis?
## urethritis?
## prostatitis?

in any case,
usually gram-negative*

# Therapy:

two 500 mg. Caplets® q.i.d
(initial adult dose)

# NegGram

Brand of

## nalidixic acid

a specific anti-gram-negative

## eradicates most urinary tract infections...

- Low incidence of untoward effects; no fungal overgrowth, crystalluria, ototoxic or nephrotoxic effects have been observed.
- "Excellent" or "good" response reported *in more than 2 out of 3* patients with either chronic or acute gram-negative infections.[1]

*As many as 9 out of 10 urinary tract infections are now caused by gram-negative organisms: E. coli, Klebsiella, Aerobacter, Proteus, Paracolon or Pseudomonas[2]... However, infections of the urethra and prostate caused by non-gonococcal gram-negative organisms are believed to be less prevalent.

**Indications:** Urinary tract infections caused by gram-negative and some gram-positive organisms.

**Side effects:** Mainly mild, transient gastrointestinal disturbances; in occasional instances, drowsiness, fatigue, pruritus, rash, urticaria, mild eosinophilia, reversible subjective visual disturbances (overbrightness of lights, change in visual color perception, difficulty in focusing, decrease in visual acuity and double vision), and reversible photosensitivity reactions. Marked overdosage, coupled with certain predisposing factors, has produced brief convulsions in a few patients.

**Precautions:** As with all new drugs, blood and liver function tests are advisable during prolonged treatment. **Pending further experience, like most chemotherapeutic agents, this drug should not be given in the first trimester of pregnancy. It must be used cautiously in patients with liver disease or severe impairment of kidney function.** Because photosensitivity reactions have occurred in a small number of cases, patients should be cautioned to avoid unnecessary exposure to direct sunlight while receiving NegGram, and if a reaction occurs, therapy should be discontinued. The dosage recommended for adults and children should not arbitrarily be doubled unless under the careful supervision of a physician. Bacterial resistance may develop.

When testing the urine for glucose in patients receiving NegGram, Clinistix® Reagent Strips or Tes-Tape® should be used since other reagents give a false-positive reaction.

**Dosage: Adults: Four Gm. daily by mouth (2 Caplets® of 500 mg. four times daily) for one to two weeks. Thereafter, if prolonged treatment is indicated, the dosage may be reduced to two Gm. daily. Children may be given approximately *25 mg. per pound* of body weight per day, administered in divided doses. The dosage recommended above for adults and children should not arbitrarily be doubled unless under the careful supervision of a physician. Until further experience is gained, infants under 1 month should not be treated with the drug.**

**How supplied:** Buff-colored, scored Caplets® of **500 mg. for adults,** conveniently available in bottles of 56 (sufficient for one full week of therapy) and in bottles of 1000. **250 mg. for children,** available in bottles of 56 and 1000.

**References:** (1) Based on 23 clinical papers, 1512 cases. Bibliography on request. (2) Bush, I. M., Orkin, L. A., and Winter, J. W., in Sylvester, J. C.: Antimicrobial Agents and Chemotherapy — 1964, Ann Arbor, American Society for Microbiology, 1965, p. 722.

Winthrop

Winthrop Laboratories, New York, N. Y. 10016

# Question of the Month—?

> **"Many non-Governmental hospitals are employing physicians for many functions which were previously not performed by their full-time staff but by practicing physicians on a voluntary basis. Will this trend eventually center medical practices in hospitals?**

### Answers and Comments

George E. Schreiner, M.D. (Internal Medicine): Medical practice will eventually be carried on in whatever manner delivers the highest quality medical care on the lowest sound economic basis. Hopefully, this will be complementary, with hospitals providing specialized facilities and practicing physicians in the community utilizing those facilities on an intelligent referral basis. When practicing physicians shut off their telephones for the weekend with advice for their patients to go to a nearby emergency room, this tends to drive ordinary medical practice in the direction of the hospital. Hospital outpatient departments allow patients to wait 4–6 hours for medical care. This tends to drive the patients to a private physician at any financial sacrifice. What is needed is a spirit of coöperation so that the talents of the community physician and the specialized facility of the hospital are integrated in a meaningful manner.

Irving B. Brick, M.D. (Internal Medicine): I certainly believe that the trend is more and more to center medical practices in hospitals or around hospitals. Further evidence of this trend is the construction of office buildings on the hospital grounds to be used by private practitioners. This makes available to the private practitioner affiliated with that specific hospital all of the facilities of the hospital and the advantage of proximity. The emergence of the widespread use of emergency rooms in hospitals, particularly at night and on weekends, as the center of treatment for practically anything also accentuates the hospital as the place to go for anything medical.

Benjamin Manchester, M.D. (Internal Medicine): Changing patterns in the practice of medicine have established the hospital as the institutional center of modern medical care. The startling rise in emergency room visits attests to the public's awareness of the hospital as the principal community health center. It also exposes the inadequacy or indifference of some physicians to provide medical care away from hospitals. Refusal of many to take new patients, delayed appointments by days, weeks, and even months, the endless waiting in reception rooms, cursory examinations, the irritation of assistants, telephone, and the unavailable physician certain days of the week, nights, and weekends compound the shortcomings of private practice and increase the institutionalization of medical practice.

The response of medicine to ever-increasing knowledge has been increased specialization. The explosion of medical knowledge has been so great that a physician can only hope to master a fraction of the whole.

The time has passed when any one doctor, regardless of his skills, can give proper care to any one patient with catastrophic disease. If available knowledge and skills are to provide the best medical care for a patient, division of effort is essential. Specialists in the different disciplines can attain their objective through productive association and collaboration. Hospital practice of medicine, whether by a group or housed in an adjacent office building on hospital grounds, permits medical care superior to what the independent practitioner can offer. A diversity of skills, specialized knowledge, competent paramedical aides, and expensive equipment, beyond the means of the private doctor, are available in hospitals or group practice clinics. New modalities have made yesterday's difficult diagnostic techniques routine procedures today.

The private practice of medicine as it was a generation ago is no longer possible. Maintenance of an individual office is declining as physicians realize the advantages of hospital, clinic, and group practice.

Through mass media of communication, patients are becoming more sophisticated and are more aware of the potential benefits of modern medicine, and they are more eager to receive those benefits.

Sociologic and economic factors combined with scientific and technologic advances demonstrate that the very best in medical care must be available to all our people. It is to be found in hospital-based or group practice clinics of specialists. This trend is on the increase. In 1931 84 per cent, in 1960 45 per cent, and in 1965 only 37 per cent of physicians were in general practice. The American Society of Internal Medicine estimates that annually 10 per cent of physicians leave solo practice and join with other physicians to form group practice. The several hundred group clinics reflect the medicine of tomorrow.

The advantages and benefits of future medicine will be attained at the price of closed hospital staffs, limited hospital privileges to private—solo—physicians, personal attention, frequent office visits, and the leisure pace of medical practice of a generation ago.

Still, a catastrophic illness has not been cured by a bedside manner, nor the laying on of hands.

Jed W. Pearson, Jr., M.D. (Obstetrics-Gynecology): As long as our socioeconomic structure allows the free choice of physician, and if physicians continue to practice medicine as an art as well as a science, no institutional practice will be acceptable to the majority of private patients as a substitute for the personal physician.

In the complex structure of modern medicine there is a place for the full-time staff physician. His main interests should be research, teaching, and the care of the unusual patient. His patients should be derived mostly from consultative referrals. His remuneration should be commensurate with that of the average practicing physician in the community.

Collection of fees by the hospital from an unrestricted private practice of a full-time staff member in order to subsidize his salary as well as other institutional expenses is a source of conflict between institutional medicine and private practice. This conflict should be faced promptly by organized medicine for the benefit of all concerned.

James R. Snyder, M.D. (Medical Education): Our program at Doctors Hospital has been going very well. It is being actively supported by the attending and resident staffs and its effect has been to develop and solidify at our hospital the concept of an active training program in medicine.

**If any members have dissenting views, your Editorial Staff will be pleased to receive and publish them.**

## Tuberculin Testing and Vaccine Administration

Much information has accumulated concerning the effect of vaccines and infectious diseases on the tuberculin reaction. Vaccines known to cause depression of the tuberculin reaction are: measles vaccine (both killed and live), oral polio vaccine, and yellow fever vaccine. Diseases showing the ability to depress the tuberculin reaction are: measles and rubella (including gamma globulin modified measles), chickenpox, pertussis, scarlet fever, and influenza.

Thus, it is recommended that tuberculin tests be given and read before the above vaccines are administered or be delayed for a variable period of time after vaccine administration or disease exposure. The following schedule is offered as a general guide in this regard.

| Vaccine or Disease | Time Period in Relation to Tuberculin Test Administration |
|---|---|
| Measles vaccine (includes live vaccine with or without gamma globulin and also killed vaccine) | Delay testing for a minimum of 6 weeks after immunization |
| Oral polio vaccine | Tuberculin test and read within 1 month after ingestion of vaccine, otherwise withhold testing for 2 months (5 to 8 weeks after OPV ingestion is time when tuberculin depression takes place) |
| Chickenpox | Delay tuberculin testing during the incubation period (2 to 3 weeks), if known exposure has occurred, and for 2 weeks after onset of the rash |
| Measles | Delay tuberculin testing during the incubation period (2 weeks), if known exposure has occurred, and for 4 weeks after onset of rash |

# Fox Rabies in the District of Columbia

During July and August of this year, there were 2 confirmed cases of fox rabies in the District of Columbia. These were the first reports of rabies within the District in 19 years. In view of the known high incidence of fox rabies in neighboring areas of Virginia and the possibility of migration of foxes across the Potomac River, as well as the possibility of transfer of rabies virus from foxes to other species of wild and domestic animals and to man, it is advisable to review at this time the present recommended treatment of animal bites and rabies prophylaxis. The following is the report of the Public Health Advisory Committee on Immunization Practices of February 1967 setting forth its recommendations on rabies treatment in the United States.

## Rabies Prophylaxis

Although cases of rabies in humans are rare in the United States, thousands of persons receive rabies prophylaxis each year. The following approach to prevention is based on a contemporary interpretation of both the risk of infection and the efficacy of treatment and incorporates the basic concepts of the WHO Expert Committee on Rabies.[1]

The problem of whether or not to immunize those bitten or scratched by animals suspected of being rabid is a perplexing one for physicians. All available methods of systemic treatment are complicated by numerous instances of adverse reactions, a few of which have resulted in death or permanent disability. Furthermore, the decision must be made immediately because the likelihood that any prophylactic measure will contribute to the prevention of rabies diminishes rapidly as the interval between exposure and treatment increases.

## Rationale of Treatment

Every exposure to possible rabies infection must be individually evaluated. In the United States, the following factors should be considered before specific antirabies treatment is initiated:

*Species of biting animal involved.* Carnivorous animals (especially skunks, foxes, coyotes, raccoons, dogs and cats) and bats are more likely to be infective than other animals. Bites of rodents seldom, if ever, require specific antirabies prophylaxis.

*Circumstances of the biting incident.* An unprovoked attack is more likely to mean that the animal is rabid. (Bites during attempts to feed or handle an apparently healthy animal should generally be regarded as provoked.)

*Extent and location of bite wound.* The likelihood that rabies will result from a bite varies with its extent and location. For convenience in approaching management, 2 categories of exposure are widely accepted:

Severe: Multiple or deep puncture wounds, and any bites on the head, face, neck, hands, or fingers.

Mild: Scratches, lacerations, or single bites on areas of the body other than the head, face, neck, hands, or fingers. Open wounds, such as abrasions, which are suspected of being contaminated with saliva also belong in this category.

*Vaccination status of the biting animal.* An adult animal immunized properly with 1 or more doses of rabies vaccine has only a minimal chance of developing rabies and transmitting the virus.

*Presence of rabies in the region.* If adequate laboratory and field records indicate that there is no rabies infection in a domestic species within a given region, local health officials may be justified in taking this into consideration in any recommendations concerning antirabies treatment following a bite by that species.

## Management of Biting Animals

A dog or cat that bites a human should be captured, confined, and observed by a veterinarian for at least 5 days, preferably 7 to 10. Any illness in the animal should be reported immediately to the local health department. If the animal dies, the head should be removed and shipped under refrigeration to a qualified laboratory for examination. Because clinical signs of rabies in a wild animal cannot be reliably interpreted, the animal should be killed at once and its brain examined for evidence of rabies.

## Local Treatment of Wounds

Immediate and thorough local treatment of all bite wounds and scratches is perhaps the most effective means of preventing rabies. Experimentally, the incidence of rabies in animals can be markedly reduced by local therapy alone.

First-aid treatment to be carried out immediately: Copious flushing with water alone, soap and water, or detergent and water.

Treatment by or under direction of a physician:

1. Thorough flushing and cleansing of the wound with soap solution. Quaternary ammonium compounds may also be used.*

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* All traces of soap should be removed before quaternary ammonium compounds are applied because soap neutralizes their activity.

2. If antirabies serum is indicated, a portion of the total dose should be thoroughly infiltrated around the wound. As in all instances in which horse serum is used, a careful history should be taken and tests for hypersensitivity performed.[2]
3. Tetanus prophylaxis[2] and measures to control bacterial infections as indicated.
4. Suturing of wound or other form of primary closure is not advised.

### Post-exposure Prophylaxis

#### ACTIVE IMMUNIZATION

*Rabies vaccine preparations.*
Duck Embryo Vaccine (DEV)
Nervous Tissue Vaccine (NTV)

*Effectiveness of vaccines in humans.* In the United States comparative effectiveness of vaccines can only be judged by frequencies of failure to prevent disease. During the years 1957 through 1967 when both vaccines were available, there were 6 rabies deaths among the 117,700 NTV-treated persons (1:19,600) and 7 deaths among the 172,000 treated with DEV (1:24,500).

*Reactions.* Erythema, pruritis, pain, and tenderness at the site of inoculation are common with both DEV and NTV. Systemic responses, including low grade fever, or rarely shock, may occasionally occur late in the course of therapy with either vaccine, usually after 5 to 8 doses. In rare instances, serious reactions have occurred after the first dose of DEV or NTV, particularly in persons previously sensitized with vaccines containing avian or rabbit brain tissue.

Neurologic complications associated with DEV have been reported for 1 of every 25,000 persons treated. One possibly related death has occurred among some 172,000 who have received DEV since its introduction.

*Choice of vaccine.* Rates of treatment failures with the 2 vaccines are not significantly different; therefore, the lower frequency of central nervous system reaction with DEV makes it preferable to NTV.

*Schedule for vaccine use.* Primary course: At least 14 single, daily injections of vaccine in the dose recommended by the manufacturer. These should be given subcutaneously in the abdomen, lower back, or lateral aspect of thighs; rotation of sites is recommended.

For severe exposures, 21 doses of vaccine are recommended. These may be given as 21 daily injections or 14 doses during the first 7 days (either 2 separate injections or a double dose), the remaining doses given singly during the next 7 days.

Booster immunization: Two booster doses, one 10 days and the other at least 20 days after completion of the primary course. The 2 booster doses are particularly important if antirabies serum was used in the initial therapy.

*Precautions.* When rabies vaccine must be given to a person with a history of hypersensitivity, especially to avian or rabbit tissues, antihistaminic drugs should be used. Epinephrine is helpful in reactions of the anaphylactoid type. If serious allergic manifestations preclude continuation of prophylaxis with one vaccine, the other may be used.

When meningeal or neuroparalytic reactions develop, vaccine treatment should be discontinued altogether. Corticotrophin or corticosteroids are used for such complications.

#### PASSIVE IMMUNIZATION

Hyperimmune serum has proved effective in preventing rabies. Its use in combination with vaccine is considered the best post-exposure prophylaxis. However, the only preparation of antirabies serum now available in the United States is of equine origin. Because horse serum induces allergic reaction in at least 20 per cent of those receiving it, its use must be limited.

Hyperimmune serum is recommended for most exposures classified as severe, and for all bites by rabid animals, wild carnivores, and bats. When indicated, antirabies serum should be used regardless of the interval between exposure and treatment.

The dose recommended is 1,000 units (1 vial) per 40 pounds of body weight. A portion of the antiserum is used to infiltrate the wound, and the remainder administered intramuscularly. As previously noted, a careful history must be obtained and appropriate tests for hypersensitivity performed.*

### References

1. Technical Report Series No. 321, WHO Expert Committee on Rabies, Fifth Report, 1966.
2. Recommendation of the Public Health Service Advisory Committee on Immunization Practices: Diphtheria, Tetanus, and Pertussis Vaccines—Tetanus Prophylaxis in Wound Management. Morbidity and Mortality Weekly Report, 1966, 15, no. 48, week ending December 3, 1966.

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* A guide for use of animal serum is included in the recommendation for tetanus prophylaxis in wound management prepared by the PHS Advisory Committee on Immunization Practices.[2]

# Let's be specific about Campbell's Soups... and *reducing diets*

Calorie content of Campbell's Soups

There are more than 30 million people in America who are overweight. During the next year, you probably will see more than 1,000 of them in your own practice.

One good way to help these patients is to give them a reducing diet based on ordinary eating patterns.

Campbell has prepared a sensible plan for weight control based on ordinary eating patterns. The plan consists of a patient instruction booklet and a set of menus which provide approximately 1,200 calories daily. The menus are balanced to provide the minimum daily requirements of nutrients.

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Pneumococci
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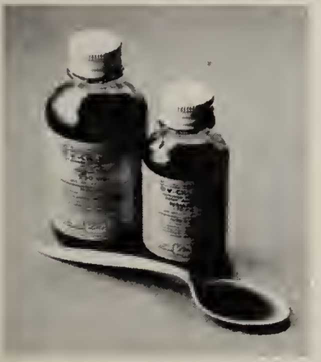
# V-Cillin K® provides dependable oral antibacterial therapy

## because it combines a high degree of activity...

V-Cillin K has been shown to be effective in the treatment of streptococcus and pneumococcus infections as well as infections caused by sensitive strains of staphylococci. It may be used for the prophylaxis of streptococcus infections in patients with a history of rheumatic fever and for the prevention of bacterial endocarditis after tonsillectomy in patients with a history of rheumatic fever or congenital heart disease.

## with high blood levels, even when taken with food

V-Cillin K is stable in acid and immediately soluble. High serum levels, therefore, are reached rapidly. Because it is acid stable, V-Cillin K is well absorbed even when taken close to mealtime. These desirable properties help make V-Cillin K a dependable penicillin for oral use.



**V-Cillin K®** Lilly 701297

**Potassium Phenoxymethyl Penicillin**

Now available: V-Cillin K®, Pediatric, for Oral Solution, 250 mg. (400,000 units) per 5 cc. of solution.

*(See next page for prescribing informatio*

# New 500 mg. tablets...a more convenient way to give high doses

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TABLETS No. 1632
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500 mg. (800,000 Units)
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**Description:** V-Cillin K is the potassium salt of V-Cillin® (phenoxymethyl penicillin, Lilly). This chemically improved form combines acid stability with immediate solubility and rapid absorption. Higher serum levels are obtained more rapidly with this penicillin than with equal oral doses of penicillin G. The higher serum levels and acid stability of V-Cillin K make it a more dependable penicillin for oral use.

V-Cillin K, Pediatric, is an oral solution of clinically proved V-Cillin K in teaspoon dosage form. When mixed as directed, each 5 cc. (approximately one teaspoonful) will contain 125 mg. (200,000 units) phenoxymethyl penicillin as the potassium salt.

**Indications:** V-Cillin K has been shown to be effective in the treatment of streptococcus, pneumococcus, and gonococcus infections as well as infections caused by sensitive strains of staphylococci. It may be used for the prophylaxis of streptococcus infections in patients with a history of rheumatic fever and for the prevention of bacterial endocarditis after tonsillectomy and tooth extraction in those patients with a history of rheumatic fever or congenital heart disease.

**Contraindication:** V-Cillin K should not be administered to a patient with a history of penicillin hypersensitivity.

**Warnings:** In rare instances, the use of penicillin may cause acute anaphylaxis which may prove fatal unless promptly controlled. This type of reaction appears more frequently in patients with a history of sensitivity reactions to penicillin and in those with bronchial asthma or other allergies. Resuscitative drugs should be readily available for emergency administration. These include epinephrine and pressor drugs (as well as oxygen for inhalation) for relief of immediate allergic manifestations and antihistamines and corticosteroids for delayed effects.

**Precautions:** V-Cillin K should be used cautiously, if at all, in a patient with a strongly positive history of allergy.

In prolonged therapy with penicillin, and particularly with hig parenteral dosage schedules, frequent evaluation of the renal an hematopoietic systems is recommended.

In suspected staphylococcus infections, proper laboratory studie (including sensitivity tests) should be performed.

The use of penicillin may be associated with the overgrowth c pencillin-insensitive organisms. In such cases, its administration shoul be discontinued, and appropriate measures should be taken.

**Adverse Reactions:** Although serious allergic reactions are much le common with administration of oral penicillin than with intramuscul forms, manifestations of penicillin allergy may occur.

Penicillin is a substance of low toxicity, but it does possess a signi cant index of sensitization. The following hypersensitivity reactio associated with the use of penicillin have been reported: skin rash ranging from maculopapular eruptions to exfoliative dermatitis; ur caria; and reactions resembling serum sickness, including chills, feve edema, arthralgia, and prostration. Severe and often fatal anaphylax has occurred (see Warnings). Hemolytic anemia, leukopenia, thro bocytopenia, and nephropathy are rarely observed side-effects ar are usually associated with high parenteral dosage.

**Administration and Dosage:** For Tablets V-Cillin K and for V-Cillin Pediatric, the usual dosage ranges from 125 mg. (200,000 units) thr times a day to 500 mg. (800,000 units) every four hours. For infan the daily dosage may be 50 mg. per Kg. of body weight divided in three doses.

Beta-hemolytic streptococcus infections without associated ba teremia may be treated with 200,000 to 400,0000 units three times day. Therapy should be continued for a minimum of ten days to preve development of rheumatic fever and/or other serious complicatio Dosage for routine streptococcus prophylaxis in patients with a histo of rheumatic fever or congenital heart disease may be 200,000 un once or twice daily. When such patients undergo tonsillectomy, too extraction, or other minor surgery, the prophylactic dose should l 500,000 units every six hours given two days prior to surgery and f two days postoperatively. If oral medication is not feasible on the d of surgery, parenteral therapy should be considered. Mild to mod ately severe pneumococcus pneumonia has been treated effective with 250 mg. every six hours.

In staphylococcus infections, 400,000 units or more should be giv every six to eight hours in conjunction with indicated surgical proc dures.

For gonorrhea in males, 500 mg. (800,000 units) every four hours f three doses may be employed; in females, 500 mg. every four hou for six doses are recommended. Refractory infections generally respo to a second treatment three to four days following completion of t first. Treatment of gonorrhea with severe complications should l individualized, with prolonged and intensive treatment. Patients with suspected lesion of syphilis should have a dark-field examination b fore receiving penicillin and monthly serologic tests for a minimum three months.

**How Supplied:** Tablets V-Cillin K, U.S.P., 125 mg. (200,000 units), bottles of 50 and 100; and 250 mg. (400,0000 units) and 500 m (800,000 units), in bottles of 24 and 100.

V-Cillin K, Pediatric, for Oral Solution, 125 mg. (200,000 units) p 5 cc. of solution, in 40, 80, and 150-cc.-size packages. [0320

*Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana 46206.*

Lilly

7012

# Policy Statement on Venipuncture and Administration of Intravenous Fluids by Nurses*

Whereas, It is recognized that under controlled conditions in many parts of the District of Columbia qualified nurses have been performing venipuncture and administering fluids intravenously, and

Whereas, Because of the law and its interpretations there have been years of inconclusive discussion concerning the nurse's legal right to perform the procedure of venipuncture and administration of intravenous fluids; therefore,

With the objective of protecting the patient, the doctor, the nurse, and the hospital or agency, the Medical Society of the District of Columbia, the Hospital Council of the National Capital Area, Inc., and the District of Columbia Nurses' Association acknowledge that it is proper practice and sound procedure for licensed professional nurses to perform venipuncture and administer fluids intravenously if all the criteria set forth below are met:

1. The nurse has had special competent instruction and supervised practice in performing the procedures.
2. The nurse performs the procedures upon the order of a licensed physician for a specific patient.
3. The procedures are limited to administration by venipuncture only. Nurses should not perform acts of minor surgery, such as "cut-downs."
4. Where the procedures are to be performed in a hospital or any other organized health agency they must be performed within the framework of regulations established by a committee composed of authorized representatives from administration, medical staff, and nursing service. This committee will have the responsibility for written statement, publication, and periodic revision of policies. These policies are to be made available to the entire medical and nursing staff.
5. It is the jurisdiction of that committee in a hospital or organized health agency to:
   a. Decide if the nurses in the hospital or agency may perform venipuncture for the purpose of administering intravenous fluids and/or withdrawing blood.
   b. Delineate the types of fluids (including blood) or medications that nurses may administer intravenously, and delineate the circumstances under which blood may be withdrawn.
   c. Determine the content of proper instruction and extent of supervised practice required.
   d. Establish in-service teaching and supervised practice of the procedures for all nurses who will be required to perform the procedures.
   e. Determine whether physician's orders should be written or oral (such determination to be consistent with the hospital or agency's rules regarding written confirmation of oral orders).
   f. Publish and maintain a roster, currently accurate, of those nurses who have successfully completed the required instructions and practice and are qualified to perform the procedures.

It is hereby recommended that consideration be given by the professional nursing schools to include the teaching of these procedures in the curriculum.

Addenda: All nurses should be aware that any statement of policy made by professional organizations or by an employing agency does not relieve the individual nurse of the responsibility for her own acts and that the nurse is liable for her own acts if she is negligent. However, this statement of policy will provide the nurse with guidelines by setting forth specific information which these responsible groups recognize as proper practice and sound procedure.

It is recognized that the final decision in any interpretation of the law is the jurisdiction of our courts.

## Self-medication

Self-medication is an especial hazard for the physician so far as drug dependence is concerned. A successful GP suffered severe abdominal pain and took Demerol® for relief. By the time he had learned of the nature of his problem he was physically dependent.

Committee on Problems of Drug Dependence
*Washington Psychiatric Society*

N. B. The Committee would appreciate it if members of the D. C. Medical Society will comment on or relate their experiences concerning problems of drug abuse or misuse.

---

* This joint statement on venipuncture and the administration of intravenous fluids by licensed professional nurses practicing in the District of Columbia, prepared by the Medical Society of the District of Columbia, the Hospital Council of the National Capital Area, Inc., and the District of Columbia Nurses' Association, was approved by the Executive Board of the Medical Society of the District of Columbia at its meeting, June 26, 1967.

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# Health Dept. Notes

### Birth Control Program

The Birth Control Program, operated by the D. C. Department of Public Health, has been functioning for 3½ years. A review of the program shows: participation exceeds expectations, the number of recipients of services is on the increase, and the annual appropriation of funds to carry on the program has reached more than ⅓ million dollars.

In April 1964 the program became operational with an appropriation from Congress of $1,000 for printing and distributing birth control materials through public maternity clinics in the District of Columbia. An additional $24,000 was then authorized for the purchase of birth control materials for a pilot program directed to about 2,400 women.

The program in fiscal year 1966 was financed with a total of $236,452, including $87,411 in District funds, $109,241 in Federal monies, and $39,800 for studies. In fiscal year 1967 appropriations for the program included $214,996 in District funds, $109,241 in Federal funds, and $39,800 for studies, for a total of $364,037. All Federal monies come from the Children's Bureau of the Department of Health, Education, and Welfare.

During the first 3 years of operation 11,604 women were registered (new admissions) in the program. New admissions for the first 3 months of 1967 totaled 1,210, compared with 1,029 for the same period in 1966. The number of visits by patients for the first half of fiscal year 1967 totaled 16,019, compared with 7,991 for the same period of fiscal year 1966.

There is no fiscal eligibility requirement for the program. Participation is entirely voluntary on the part of the patient, and the method of birth control used is determined in conference between the patient and her physician. The methods employed are oral tablets, intra-uterine devices, vaginal foams, creams and jellies with or without diaphragm, and instructions in the rhythm method.

Increased participation in the program is attributed to relaxation of eligibility, expansion of facilities, establishment of a Public Health Birth Control Information Center, and added support from the Health Education and Information Division of the Health Department.

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When the program was established only married women who had delivered within 90 days and were patients in the maternity clinics of the Health Department were eligible. Shortly thereafter the program was expanded to include unmarried women who had delivered within 90 days, and subsequently to all married women who had children. In October 1966 eligibility was relaxed to include all unmarried women who had children. In February of this year married women who have not had children were added to the eligibility list. Thus, only 1 category—unmarried women who have not had children—are excluded from birth control services of the Health Department.

The Health Department currently operates 11 birth control clinics and will soon be opening another clinic.

The Birth Control Information Center was established in the Gales Building with a publicized telephone number—737-5557. When a call pertaining to other than registration or appointments is received, it is referred to a nurse in the birth control clinic. If a query requires answering by a physician, it is referred to the doctor on duty.

Four public health educators and 5 public health education aides are assigned to the Maternity and Infant Care Program, which includes birth control, and work directly with residents of the District and community organizations. Health educators and health education aides have conducted door-to-door campaigns to inform residents of new clinics. One Spanish-speaking aide assists with interviewing Spanish-speaking people at one of the mobile clinics.

Local radio and television stations have used spot announcements supplied by the Health Department, and staff personnel have appeared on both radio and television programs explaining the District's birth control program.

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## Report on Postgraduate Course on Sports

The Postgraduate Course on Sports, presented by the Committee on Sports Medicine of the American Academy of Orthopaedic Surgeons in Oklahoma City, August 14, 15 and 16, was, I understand, the first of its kind to be put on by the Academy. Oklahoma City was specifically selected out of honor to Dr. Don O'Donohue, under whose stimulation the Committee was initially organized.

The Monday morning symposium dealt with the "throwing arm." The subjects presented included shoulder-joint muscle injuries, epicondylitis, the aging pitcher, and injuries to the hand in athletes.

Movies illustrated the style of pitching. Fast hard pitchers gradually changed their style, as they became older, from a direct overhand to a slightly sidearm delivery. Following a study of 50 professional pitchers Dr. Joe King reported that 83 per cent of them had changes in the elbow, detectable by X-ray films, by the time they were 26 to 33 years of age.

Traction spurs were frequently noted extending from the medial ulnar notch. It was emphasized that surgery on these elbows be deferred unless the pitcher has lost his effectiveness. Dr. McDonald, while discussing the aging pitcher, stated that he has yet to see a professional pitcher rehabilitated after surgery in which the deltoid was detached from the clavicle. He advocated the use of a muscle-splitting incision if at all possible.

The program on Tuesday included a history and logistics of the Olympic games presented by Dr. Allen Ryan. Other subjects that morning were the prevention of heat illness in football players, the treatment of gastroenteritis in traveling athletes, cardiorespiratory problems in athletes, and telemetry in the study of the heart in athletes.

The prevention of heat illness involves the recognition of heat stroke and heat exhaustion, the importance of replacing adequate water and salt, as well as noting the weights of the players both before and after practice. The importance, during practice, of measuring wet bulb temperatures by means of a sling psychrometer was discussed. This reading as compared to the dry bulb reading relates to relative humidity, and it is believed that in most circumstances this is an ideal indicator as to whether it is safe or not for practice to be conducted.

In his discussion of altitude at the Olympic games, Dr. Ryan observed that after training for a while at high altitudes the athlete's performance when he returned to lower levels was appreciably better than it was prior to training at the higher altitudes.

Dr. Donald Slocum discussed the mechanics of the running gait. He noted that the great runners run so that a plumb line would drop from the ear through the groin. If they tended to lean forward, they actually impeded their running.

Wednesday morning was devoted to injuries of the knee. Dr. Fred Reynolds, a physician for the St. Louis Cardinals, gave an excellent discussion of the diagnosis of acute ligament injuries. He reviewed the function of the medial collateral ligament and anterior cruciate ligaments and the disability when one or both were injured.

Dr. James Nicholas revealed that he has been doing arthrograms by the technique noted in the *American Journal of Roentgenology* in July 1966. His statistics, especially in locating double menisci injuries and posterior remnant retention, impressed everyone present.

Dr. O'Donohue is to be congratulated for hosting in a magnificent manner an extremely informative program.

Stanford Lavine, M.D.
*Vice Chairman, Committee*
*on Medical Aspects of Sports*

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## AMA Reaffirms Support of All Nursing Education Programs

The House of Delgates of the American Medical Association has reaffirmed the Association's support of all forms of nursing education programs. At its June 1967 biannual session in Atlantic City, the House adopted the following statement on nursing education:

Whereas, The American Medical Association is on record to "continue its support of all current nationally approved educational programs for nurses"; and

Whereas, The national trend which is supported by the professional nurses' associations appears to be the gradual phasing out of the diploma schools of nursing and the transfer of nursing education to collegiate institutions; and

Whereas, 70 per cent of nursing care at the present time is rendered by graduates of diploma schools with the demand for such nurses continuing to exceed the supply; and

Whereas, There is general professional agreement on the need for inclusion of nursing education in community health planning with provision for greater use of in-hospital training as well as training in collegiate institutions; therefore be it

*Resolved*, That the American Medical Association reaffirms its support of all forms of nursing education including baccalaureate, diploma, associate, and practical nurse education programs; and be it further

*Resolved*, That those hospitals that conduct diploma schools of nursing be commended for the great contribution being made by these institutions to the health needs of the Nation; and be it further

*Resolved*, That such hospitals be urged to continue their schools and increase enrollment while allowing the individual to choose the kind of nursing education he or she desires; and be it further

*Resolved*, That the American Medical Association take appropriate action in consultation with professional nurses' associations and the American Hospital Association to encourage increasing enrollment in diploma schools and at the same time improve educational standards.

## Patients Needed for Studies of Infectious Diseases

The Laboratory of Clinical Investigations, National Institute of Allergy and Infectious Diseases, National Institutes of Health, has initiated a study of infectious mononucleosis, infectious lymphocytosis, and related diseases. Patients with acute infectious mononucleosis-like illnesses with clinical manifestations of fever, malaise, lymphadenopathy, pharyngitis, and peripheral lymphocytosis with atypical forms are being sought.

Areas of investigation are the virologic, hematologic, and immunologic manifestations of these disease syndromes:

*Virologic studies.* Attempts will be made to demonstrate or isolate an infectious agent with a variety of newly developed tissue culture techniques.

*Hematologic studies.* The function of the atypical lymphocyte will be studied in terms of DNA, RNA, and specific immunoglobulin synthesis.

*Immunologic studies.* Origin and classification of the heterophil antibody, acute phase proteins, and serum immunoglobulins, as well as the production of the specific agglutinins associated with acute hemolytic anemia will be studied.

Upon completion of their studies the patients will be returned to the care of their referring physicians, to whom complete narrative summaries will be sent.

Physicians interested in referring patients to the study are asked to contact the Acting Clinical Director, Laboratory of Clinical Investigations, National Institute of Allergy and Infectious Diseases, Bethesda, Md. 20014; telephone: (301) 656-4000, Ext. 64963.

## Smoking in Educational Institutions

Smoking is not allowed in classrooms and laboratories of more than 90 per cent of colleges and universities polled in a Nation-wide survey. A significant number, however, permit cigarette vending machines and the direct sale of cigarettes on campus. More "startling" is the extent to which smoking is permitted in college and university health services.

These are among the findings of a study of smoking policies of these institutions conducted by the National Interagency Council on Smoking and Health and announced, March 31, at the 45th Annual Meeting of the American College Health Association in Washington, D. C.

Reporting on the study, Dr. Harold S. Diehl, the Council's Vice Chairman and a Vice President of the American Cancer Society, said its purpose was to gather information on the factors and influences in the college environment that might encourage students to start smoking or to continue a habit already begun.

Questionnaires were sent to presidents of 2,044 institutions of higher learning. Completed replies were received from 1,232, or 60.3 per cent.

Following are highlights:

— Small colleges generally are more concerned and doing more about the smoking problem than large institutions with 10,000 or more students.

— Teachers' colleges stand uniquely alone in their unanimity in prohibiting smoking by students or faculty in classrooms and laboratories.

— Cigarette vending machines on campus were reported by 85 per cent of the institutions with 3,000 students or over and the direct sale of cigarettes by 76 per cent of the institutions of the same size, yet cigarette advertising has been removed from campus publications, sports programs, and sponsored sports events.

— Although students on a few campuses have insisted on retaining cigarette vending machines, there are encouraging indications that students might support a stronger stand by their colleges on smoking. At Princeton, for example, 93 per cent of the freshman class did not smoke, and 43 per cent of those who do smoke said they wish to discontinue.

"These are hopeful developments," said Dr. Diehl. "Nevertheless, they present a challenge to the American College Health Association and other members of the National Interagency Council. Our task is to see that the percentage of non-smoking undergraduates increase and that those who smoke and wish to discontinue are given help."—News release, American College Health Association, March 31, 1967.

# DOCPAC Briefs

### or

### Why Bother?

Since Medicare legislation was passed and is now the law of the land, comments of "What's the use?" or "Why bother?" are sometimes heard when conversing with physicians about joining DOCPAC (the District of Columbia Political Action Committee) and also becoming active in the political party of their choice. For those who feel this way, please take a moment to read the following which appeared in *The Machinist* publication and was reprinted in the *AFL-CIO News*:

> "Union members have a right to be proud . . . over the start of the new Medicare program for those over 65.
>
> "This expansion of Social Security is the fruit of 30 years of planning, promoting, pleading and politicking by union officers, health officials, social workers, senior citizens and countless others. . . .
>
> "Medicare is a brave new step toward meeting the health needs of our Nation. But because it is a new step for the United States, many are worried that it won't work.
>
> "Much more elaborate health insurance programs already are operating successfully in other industrialized nations. There is no sound reason it shouldn't work well here. . . .
>
> "Our biggest regret is that the Medicare program falls so far short of real needs. There are no provisions, for example, for glasses or hearing aids or dental plates that the elderly so often cannot afford no matter how desperate their need.
>
> "And, there is no national health insurance for anyone under 65. But now that may be possible.
>
> "National health insurance for everyone as a part of the Social Security program was first recommended to Congress in 1935 by President Franklin D. Roosevelt. . . .
>
> "In 1943 the Wagner-Murray-Dingell bill was introduced in Congress calling for expansion of the Social Security Act to include national health insurance for all.
>
> "In 1964, the Senate and House passed conflicting measures and the bill was defeated. . . .
>
> "But public demand for the legislation continued to mount. Under the leadership of President Johnson the bill became law in 1965—after 30 years of effort.
>
> "Let's hope the extension of Medicare to the rest of the country will come more quickly."

Will it? Undoubtedly—if we refuse to take an active part in electing responsible individuals to the U. S. Senate and House of Representatives.

William H. Cooper, M.D.
*Chairman, D. C. Political Action Committee*

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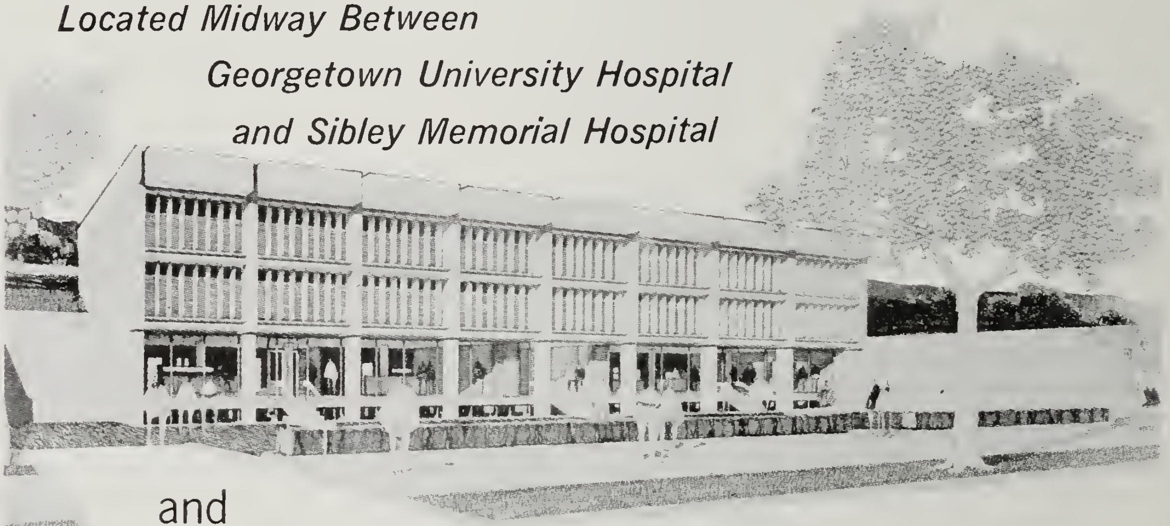

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# DORSEY Season

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this issue: smog, smaze or smust...

# Smog, smaze or smust...effects of air pollution on upper respiratory tract

Nathan Flaxman, M.D., Diplomate, American Board of Internal Medicine, Chicago, Illinois

In Los Angeles it is *smog* (smoke and fog). In New York City *smaze* (smoke and haze). In El Paso *smust* (smoke and dust). The original factor was smoke plus such natural phenomena as fog, haze and dust, but air pollution has mushroomed from a smoke problem in our industrial cities into a major economic, esthetic and public health problem that affects practically every American locality and citizen.[1,2] Respiratory disease, of course, is by far the most costly effect of air pollution, for contaminated air can aggravate our illnesses, deplete our strength and shorten our life span.[1]

The greatest problem in dealing with solid wastes is that they are not quickly returned to dust. To aid the decomposing process, the great bulk of such waste is burned, polluting our air in the process.[3] Dr. Jack McKee of the California Institute of Technology[4] has calculated that in Los Angeles County, which has more than six million people, about three pounds of gaseous wastes per person per day (on a dry-weight basis) enter the atmosphere. This is twice as much as solid refuse disposal and six times as much as the contaminants in waste water. It is estimated that in New York City, 730 pounds of pollutants, a little over half the size of a compact two-door sedan of foreign make, is annually thrown into the air for each man, woman and child in the city.[5]

Air pollution is an evident factor, not only in the common cold and upper respiratory disease, but also in chronic bronchitis,[2] pulmonary emphysema,[6] bronchial asthma,[7] pneumonitis and lung cancer.[8] Its effect on the incidence of pulmonary tuberculosis is unproved,[9] although it is conceivable that the presence of various materials polluting the air might do this. A siege of smog in Denver, the "mile high city," in December 1965 was accompanied by respiratory infection that doubled normal absentee rates in schools, factories and city government.[10]

While air pollution is only one factor, it has become important in the causes of most of the afflictions of the respiratory tract. This has been shown not only by the Denver occurrence, but also by detailed study[2] of respiratory illness in a small group of 313 men

from October 1962 to May 1963 when there were 202 episodes involving the upper respiratory tract. The attack rate of illness was related in time to increased concentration of both smoke and sulphur dioxide in the atmosphere of the district in which the men lived.

Other factors often mentioned, include exposure to those who have colds, exposure to extreme changes of temperature, allergy and bacterial infection. However, when low individual resistance due to lack of rest, overwork, fatigue, improper or unbalanced diet, previous illness and emotional stress are included as causes, we enter the realm of somewhat obscure relationships. Much more emphasis can be placed on the role of polluted air.

The symptoms, signs and complications of involvement of the upper respiratory tract, especially the common cold, are the same regardless of the causative factor. Swelling of the lining of the nose, the scratchy dry throat, the discharge from the nose at first watery then thicker, discolored and more tenacious, the eyes tearing, and frequent sneezing are all part of the Number 1 human ailment. Concurrent or residual sinusitis when mucus is trapped there, middle ear involvement due to interference with drainage, laryngitis and bronchitis are complications of the common cold. The primary interference is with a most important function of the nose—the cleansing of foreign matter in the first line of "air defense" to prevent it from entering the breathing tract.

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However, the diagnosis and subsequent decision on how to treat the patient so affected rests basically on the relief of symptoms that cause him the misery. The stuffed, runny nose, the clogged ears, and the harsh dry cough—all the symptoms that make common cold sufferers feel miserable and interfere with their sleep—can be alleviated with medications of the oral nasal decongestant/antihistamine combination type. The burning sensation in the throat, soreness of the chest and even chest pain can also be relieved by such medication. Rest in bed if there is fever (but confined to home at least), liberal fluids, uniformly warm surroundings and adequate humidity in the room, are all helpful adjuncts to the medication. Most common cold sufferers recover rapidly and are symptom-free in four to ten days.

Further treatment, altered by the fact that the affliction hangs on for more than the usual duration of the common cold, requires consideration of allergy, which is most frequently the prolonging factor. But air pollution itself may often be the culprit.

*(Concluded on following page)*

At the Third National Conference on Air Pollution held recently, it was emphasized that this subject had received more attention in the past four years than in all previous history. Spicer,[11] an active participant at this conference, reiterated that it behooves the practicing physician to be aware of trends in respiratory disease and to accept a major role in community action relating to air pollution and respiratory health. By taking a positive stand physicians have been instrumental in the development of antipollution legislation. An outstanding example is Los Angeles where major steps have been taken by abolishing coal burning, and even banishing oil burning, seven months a year. Natural gas must be used instead and it must be used by industry when available. Backyard incinerators have been abolished in favor of landfill disposal, and building incineration ended except for a few expensive smokeless furnaces.[10] Concerted action can be taken against particular industrial nuisances. One company that disregarded complaints discovered its error when thousands of its credit cards were returned by irate customers who decided to patronize competing companies.[12]

*Summary.* Respiratory disease is the most important and most costly effect of air pollution, whether termed smog, smaze, or smust. Air pollution is an economic, esthetic and public health problem that affects practically every American locality and citizen. New sources of air pollution are invisible and odorless, but the harmful gases and liquid droplets are there. Triggered by sunlight, some of these undergo mid-air chemical changes and the results are even more irritating to the upper respiratory tract. The symptoms, signs and complications, especially of the upper respiratory tract, can be readily aborted by modern medication but may be unduly prolonged by polluted air. In steps taken to prevent this, the practicing physician can take a major role.

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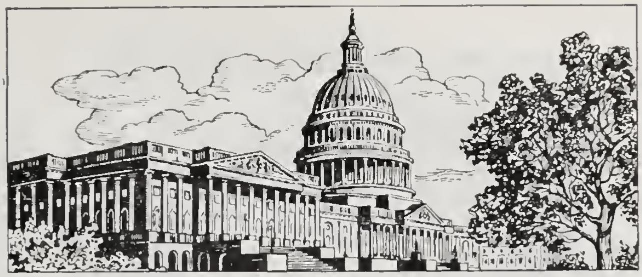

# NEWS & PERSONALS

## Meetings

**The Division of Dermatology and the Postgraduate Education Committee of Howard University College of Medicine** are presenting a Symposium on the Dermatology of the Negro at the College, Wednesday and Thursday, October 18 and 19, beginning at 9 a.m. each day. The program has been planned to include all aspects of those skin diseases which tend to afflict Negroes more than Caucasians and which might almost be said to be "peculiar" to the Negro, as well as the various pigmentary disorders, both hypopigmentation and hyperpigmentation.

Program participants will include faculty members from the Schools of Medicine of Tulane, Yale, Wayne, Johns Hopkins and Howard Universities, from Meharry Medical College, and a number of other distinguished speakers from metropolitan areas.

Program inquiries may be addressed to Dr. John A. Kenney, Jr., Chairman, Division of Dermatology, Freedmen's Hospital, Washington, D. C. 20001.

**The Clinical Meeting of the American Medical Association** will be held this year in Houston, Texas, November 26–29. As usual, a number of special conferences will be held in conjunction with the Clinical Convention.

**The Second National AMA Conference on Utilization Review** is scheduled for 9 a.m. to 5 p.m. at the Shamrock Hilton on Saturday, November 25. For further information contact the AMA Department of Hospitals and Medical Facilities.

**The Ninth National Conference on the Medical Aspects of Sports,** sponsored by the AMA under the auspices of its Committee on the Medical Aspects of Sports, will be held in Houston at the Hotel America on November 26.

As was true of the previous Conferences, the Ninth will cover a wide range of subjects of interest to those serving school and college athletic programs. Two sessions will be devoted to a series of common clinical conditions of rather variable significance in the athletic setting (e.g., gastroenteritis, concussions, genitourinary tract injuries, and rib injuries).

The Conference is open to key nonmedical athletic personnel as well as interested physicians. Those who would like to receive further information concerning the Conference should address the AMA Committee on the Medical Aspects of Sports.

**The International Society of Medical Directors of Chronic Disease Facilities** will hold an all-day meeting, November 30, in the Warwick Hotel, Houston, immediately following the AMA Clinical meeting. Dr. Bertram B. Moss, President of the newly formed Society, has extended an invitation to all medical directors of chronic disease facilities and other interested physicians to attend.

With Medicare ruling that every extended care facility must have a full-time medical director for all patients, including those not covered by Medicare, this new Society perceives its role as a central agency where this special group of physicians may come together to obtain information and discuss problems and recent developments in their field.

Inquiries regarding membership and further details of the November meeting should be directed to Miss Patricia Morgan Dorr, Executive Director, 360 North Michigan Avenue, Chicago, Ill. 60601.

**The Fourth Annual John Fitzgerald Kennedy Memorial Lecture,** presented by the Department of Pediatrics of Georgetown University School of Medicine, will be held December 8, 1967. The guest lecturer will be Dr. Norman Kretchmer, Professor and Executive Officer of the Department of Pediatrics, Stanford University School of Medicine.

# General News

**The George Washington University School of Medicine** has reinstated its **Department of Orthopedics** and named Dr. John P. Adams as its Chairman. Orthopedic surgery was a department at George Washington from 1894 to 1931; it later became a subspecialty of the Department of Surgery, where it has continued until the present

Dr. Adams joined the medical faculty of George Washington in 1953, attaining the rank of Professor of Orthopedic Surgery in 1964. He is a consultant in orthopedic surgery to Veterans Administration Hospital, Walter Reed General Hospital, Division of Indian Health (PHS), the Naval Medical Center, and Howard University, and he is chief of the Hand Clinic at D. C. General Hospital and the D. C. Division of Maternal and Child Health.

**Wyeth Laboratories** announces that applications for 2-year **Pediatric Fellowships** are available now for residencies to commence July 1, 1968. Sponsored by the Wyeth Fund for Postgraduate Medical Education, each of the fellowships provides $4,800 over 2 years toward the advanced training required for Board-certification in pediatrics. These payments are in addition to the usual stipend paid to the resident by the institutions in which they train.

Eligible to apply are interns, physicians who have recently completed an internship, research fellows, or physicians completing their tour of duty with the Armed Services or the U.S. Public Health Service. Applicants must be citizens of the United States or Canada.

A voluntary committee of distinguished pediatricians, headed by Dr. Philip S. Barba, Adjunct Professor of Pediatrics at Temple University School of Medicine and Past President of the American Academy of Pediatrics, has the responsibility of choosing the Pediatric Fellows. Applications should be sent to Dr. Barba at 120 Erdenheim Road, Philadelphia, Pa. 19118, and must be in the hands of the Committee by December 1, 1967.

**Georgetown University School of Medicine** has received a renewal grant of $17,997 from The Arthritis Foundation to continue its model program on arthritis, now in its second year. In charge of the **Arthritis Clinical Research Center** is Dr. Nathan J. Zvaifler, Associate Professor of Medicine and Director of the Division of Rheumatic Diseases.

In addition to the Clinic at Georgetown University Hospital, a Pediatric Rheumatic Disease Clinic has been established at Children's Hospital. Dr. Henry Roth, an Associate member of the D.C. Medical Society, is Assistant Program Director for the Center.

**George Washington University School of Medicine** has received a grant of $237,816 from the John A. Hartford Foundation, Inc., of New York, for furthering studies of human allergic reactions to insect stings, bites and other contacts. The 3-year study will be under the direction of Dr. Halla Brown, Professor of Medicine and Chief of the Allergy Section.

The Department of Pediatrics at **Howard University College of Medicine** held a formal opening of its **Child Development Center** on September 19. The Center will provide comprehensive, multidisciplinary diagnostic and treatment services for children who are suspected of having problems in some area of development. There is close collaboration between the Child Development Center and the Medical Genetics Unit of Howard University. The Center will serve as a training facility for students in the various disciplines related to mental retardation. Dr. Pearl L. Rosser is the Medical Director.

The Child Development Center was made possible by funds supplied by the U.S. Children's Bureau and Howard University. Directing the project is Dr. Roland B. Scott, Professor and Chairman of the Department of Pediatrics.

**George Washington University School of Medicine** has appointed **Dr. John Chandler Smith, Associate Professor of Pathology.** He comes to Washington from Western Reserve University, Cleveland, where he held Associate Professorships in Pathology and Radiology. A native of Denver, Dr. Smith received his medical degree from the University of Oregon Medical School in 1944. He is a diplomate of the American Board of Pathology in both Clinical and Anatomic Pathology, and is a member of many scientific organizations.

Two Washington hospitals have new administrators. **Sister Frances Michael** has been named **Administrator of Providence Hospital,** succeeding Sister Margaret Eileen, who has served for 6 years in the post.

The Board of Directors of **Columbia Hospital for Women** has announced the appointment of **Mr. Donald B. Scheurer as Administrator** to succeed Mr. John A. Oley, who has retired. Mr. Scheurer was associated with the Alexandria Hospital before coming to Columbia as Administrative Assistant in 1961. The following year he was appointed Assistant Administrator.

**Mr. Alan F. Ridgway** has been named **Assistant Executive Vice President of Medical Service of D. C.** He has served since 1964 as Manager of the Basic Claims Department of Group Hospitalization, Inc., which administers the Blue Cross Plan.

Succeeding Mr. Ridgway as **Manager of the Basic Claims Department of GHI is Mr. Robert L. Surdam.** This department handles more than a million physician and hospital claims annually in behalf of Washington area Blue Cross and Blue Shield subscribers.

**Two publications** have been received in the Medical Society's Executive Offices **from The Epilepsy Foundation**: "A National Directory of Clinic Facilities for the Diagnosis and Treatment of Epilepsy" and "Summaries of Articles on Juvenile Epilepsy." Both publications are available upon request to the Foundation at 1419 H Street, N.W., Washington, D. C. 20005; telephone 638-4350.

## Personals

**Dr. Naomi M. Kanof,** who resigned, July 1, after serving as Editor of *The Journal of Investigative Dermatology* for 17 years, has been honored with a special number dedicated to her. The July issue contains a section lauding her unique contributions to the *Journal* and to her specialty, dermatology. The articles were written by friends and colleagues, among them Dr. Marion B. Sulzberger, whom she succeeded as Editor, Dr. Herman Beerman, Dr. Rudolf L. Baer, Mr. William M. Passano, President of the Williams & Wilkins Company, and Dr. Eugene J. VanScott, Guest Editor. The new Editor, Dr. Richard B. Stoughton, wrote the introductory paragraphs. The issue contains some excellent photographs of Dr. Kanof, including one of her family.

**REPORTING TO THE PRESIDENT: President Lyndon B. Johnson greets Dr. Patrick J. Doyle, a member of the President's Committee on Mental Retardation, following the Committee's presentation of its first report at a White House ceremony. Dr. Doyle is a member of the Medical Society's Committee on Rehabilitation and Chronic Illness.**

**Dr. Dale C. Cameron,** Superintendent of St. Elizabeths Hospital, has resigned to take a position with the World Health Organization in Geneva, Switzerland.

Dr. Cameron came to Washington in 1945 as Assistant Chief of the Mental Health Division which later became the National Institute of Mental Health in Bethesda. He left in 1954 to become Medical Director of the Minnesota Department of Public Welfare, and returned to Washington to join the staff of St. Elizabeths in 1960. He took over as Superintendent in September 1962, succeeding Dr. Winfred Overholser, who retired.

**Dr. Lawrence S. Lilienfield,** Chairman of the Department of Physiology and Biophysics at Georgetown University School of Medicine, began a sabbatical year, October 1, which he will spend in Israel helping to establish courses in physiology at the Tel Aviv School of Medicine. In the past the Medical School in Tel Aviv provided only clinical training to graduate physicians. Beginning the fall, the School will enroll medical students and offer them courses in the basic sciences. During the year Dr. Lilienfield will continue to direct a teaching program in physiology at the University of Saigon in South Vietnam.

**Dr. Lendall C. Gay** received the 1967 Achievement Award of the Sibley Medical Association at a dinner held at the Officers' Mess of the Washington Navy Yard on May 6. The dinner was the closing event of the Annual Scientific Symposium sponsored by the Sibley medical alumni.

Dr. Gay, a native of South Carolina, has lived in Washington most of his life. He graduated from the Medical College of Virginia in 1937. He admitted his first hospital patient to Sibley and has been active at Sibley since that time, serving on the Executive Committee of the Sibley Medical Association almost without interruption since its origin and as its President in 1961.

His wife, Dr. Claudine Moss Gay, is also a practicing physician and an Active member of the D.C. Medical Society.

**Dr. Marianne Ida Schuelein** has joined the faculty of the Georgetown University School of Medicine as Assistant Professor in Pediatrics and Neurology. Dr. Schuelein is a graduate of the New York University School of Medicine, receiving her medical degree in 1959. Prior to her appointment she was a resident in neurology at Georgetown University Hospital.

# Obituaries

## Benjamin F. Weems, Jr., B.A., M.D.

(1886–1967)

Dr. Benjamin F. Weems, Jr., who had been retired from active practice since 1957, died, August 7, 1967, at the Washington Hospital Center. His home was at 3111 Chain Bridge Road, N.W.

Dr. Weems was born in Houston, Texas, September 22, 1886. He completed his early education in Houston and his undergraduate studies at Johns Hopkins University. He continued his studies in medicine at Johns Hopkins, receiving his degree in 1913. He interned at Bellevue Hospital, New York, for the next 2 years and served as resident physician for another year.

During World War I Dr. Weems was Chief Pathologist at Camp Dix, New Jersey. He went overseas in 1918 to serve as Chief Officer in the Department of Pathology and Infectious Diseases at Base Hospital No. 1 in France.

After the war Dr. Weems began the practice of internal medicine in Washington. For many years he was Chief Attending Physician at Garfield Memorial Hospital. He was on the staff of Georgetown University School of Medicine as Assistant Professor of Medicine from 1920 to 1929 and was Professor of Clinical Medicine for more than 10 years.

Dr. Weems was a member of the American Medical Association, the Johns Hopkins Medical and Surgical Society, Hippocrates-Galen Society, and an Active member of the Medical Society of the District of Columbia from 1922 to 1959.

His wife, Mrs. Helen Ellis Weems, died in 1954. He leaves 2 sons, Benjamin F. Weems III and Charles E. Weems, and a sister, Mrs. H. R. Dulany.

### Rhythm of Sexual Desire in Human Female—Cavanagh

(*Continued from page 583*)

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VAN DE VELDE, T. H.: Ideal Marriage. New York: Random House, 1957.

WRIGHT, H.: The Sex Factor in Marriage. New York. Vanguard Press, 1931.

"All Registered Nurses are Alike"

It stands to reason. They all go through the same training; they all have to pass the same tests; they all have to measure up to the same standards. Therefore, all registered nurses are alike.

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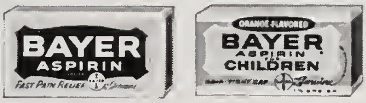
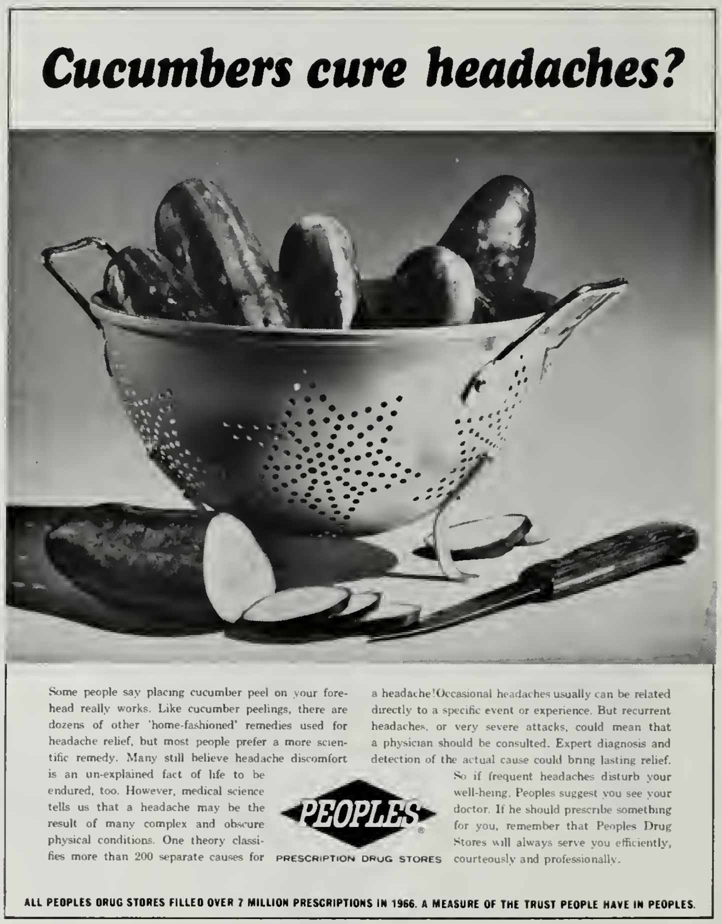
So next time you hear someone say that all aspirin tablets are alike, you can say, with confidence, that it just isn't so.

You might also say that all registered nurses aren't alike, either.



...and then there's the one about cucumbers curing headaches.



**Cucumbers cure headaches?**

Some people say placing cucumber peel on your forehead really works. Like cucumber peelings, there are dozens of other 'home-fashioned' remedies used for headache relief, but most people prefer a more scientific remedy. Many still believe headache discomfort is an un-explained fact of life to be endured, too. However, medical science tells us that a headache may be the result of many complex and obscure physical conditions. One theory classifies more than 200 separate causes for a headache! Occasional headaches usually can be related directly to a specific event or experience. But recurrent headaches, or very severe attacks, could mean that a physician should be consulted. Expert diagnosis and detection of the actual cause could bring lasting relief.

So if frequent headaches disturb your well-being, Peoples suggest you see your doctor. If he should prescribe something for you, remember that Peoples Drug Stores will always serve you efficiently, courteously and professionally.

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The nystatin can prevent overgrowth of monilia; the phosphate complex delivers tetracycline to the blood rapidly. Side effects are infrequent.

**High-Risk Patients**

Tetrex-F (tetracycline phosphate complex-nystatin) is especially useful in patients most susceptible to fungal overgrowth during tetracycline therapy: (1) the elderly or debilitated, (2) young children, (3) the diabetic, (4) those on long-term tetracycline therapy, (5) those on steroid therapy, (6) those who have had moniliasis before, and (7) pregnant patients with a history of monilial vaginitis.

When you start with economical Tetrex-F (tetracycline phosphate complex-nystatin), you can complete the full course of broad-spectrum therapy with less chance of losing control elsewhere. A good start for a healthy finish.

PRESCRIBING INFORMATION. For complete information consult Official Package Circular. *Indications:* Infections of respiratory, gastrointestinal and genitourinary tracts and skin and soft tissues due to tetracycline-sensitive organisms, in patients with increased susceptibility to monilial infections. *Contraindications:* The drug is contraindicated in patients hypersensitive to its components. *Warnings:* Photodynamic reactions have been produced by tetracyclines. Natural and artificial sunlight should be avoided during therapy. Stop treatment if skin discomfort occurs. With renal impairment, systemic accumulation and hepatotoxicity may occur. In this situation, lower doses should be used. Tooth staining and enamel hypoplasia may be induced during tooth development (last trimester of pregnancy, neonatal period and childhood). *Precautions:* Bacterial superinfections may occur. Infants may develop increased intracranial pressure with bulging fontanels. In gonorrheal therapy, serologic tests for syphilis should be conducted initially and monthly for 3 months. *Adverse Reactions:* Glossitis, stomatitis, nausea, diarrhea, flatulence, proctitis, vaginitis, dermatitis, and allergic reactions may occur. *Usual Adult Dosage:* 1 capsule q.i.d. Continue for 10 days in Beta-hemolytic streptococcal infections. Administer one hour before or two hours after meals. *Supplied:* Capsules, bottles of 16 and 100. Each capsule contains tetracycline phosphate complex equivalent to 250 mg. tetracycline HCl activity and 250,000 units of nystatin. For Oral Suspension, 125 mg. tetracycline and 125,000 u. nystatin/5 ml., 60 ml. bottles.

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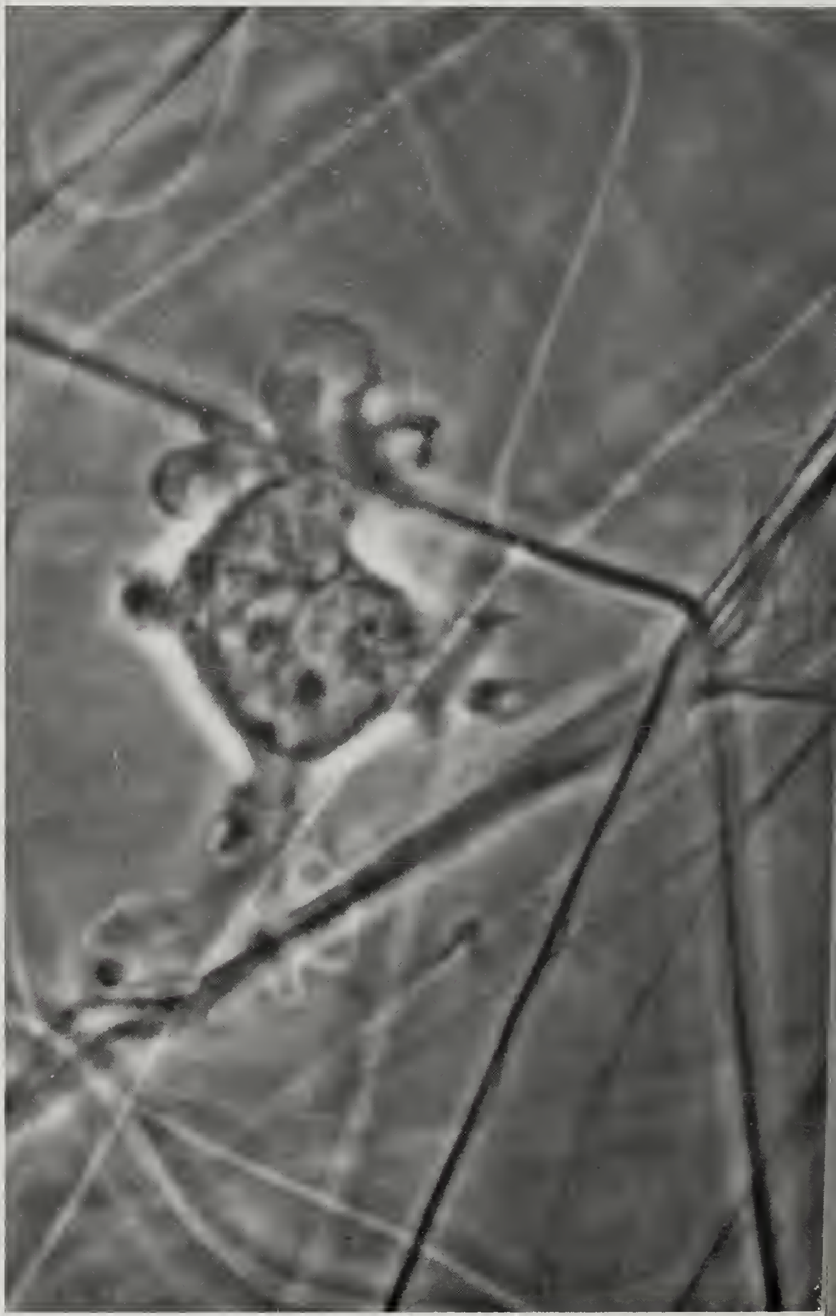
# INFLAMMATION:
# A cellular fight for life

*A SYNTEX REPORT based on recently developed hypotheses about topical corticosteroids, including the cellular theories of inflammation by Thomas F. Dougherty, Ph.D., University of Utah.*

You are looking at a fibroblast fighting for life. This cell—one of the most common found in connective tissue—has literally been poisoned by cytotoxins released from other cells that have ruptured. Soon, if the abnormal activity of this fibroblast does not cease, it, too, will rupture and die—one more casualty in the inflammatory wave of destruction precipitated by injury.

Until a short time ago no one had ever witnessed such a scene at the cellular level. Now, through advanced cinemicrographic techniques, it is possible to view and photograph the inflammatory process as produced experimentally in living animal tissue. This method permits new insight into the mechanism of inflammation and the role of corticosteroids in therapeutic management. Equally important, these techniques shed new light on factors that may make one corticosteroid more effective than another—factors that can be correlated with other chemical, biologic, and clinical parameters.

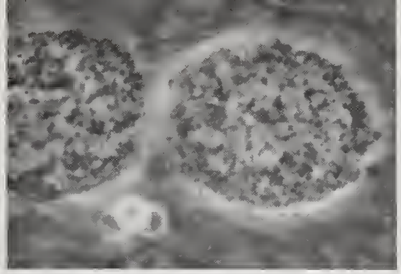


## Visual evidence of how corticosteroids influence the inflammatory reaction

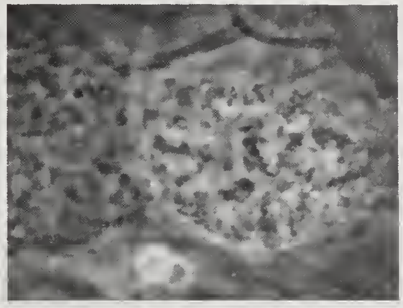
Working with phase-contrast cinemicrography on living animal tissue, Doctors Thomas F. Dougherty and David Berliner of the University of Utah College of Medicine have actually filmed cellular events that occur during the inflammatory reaction. This remarkable study* and additional work by these investigators, as well as by others, have established a new theoretical biologic basis for the antiinflammatory effect of the corticosteroids. (It must be noted that other theories, such as the lysosome or so-called "suicide bag" theory, have been postulated, although it is quite likely that there are more similarities than differences among the various theoretical models.)

## The inflammatory wave of destruction

In this investigation an injurious injection of gelatin is used to set off an inflammatory reaction in living mouse tissue. What follows is a wave of destructive cellular activity that comprises the inflammatory response to injury. Mast cells (which contain heparin, serotonin and histamine) take up water, swell and rupture, releasing their contents, which are toxic outside the mast cell wall. These toxins, in turn, cause disintegration of other cells (such as fibroblasts) and the release of additional toxic material. Capillaries, too, take up water and leak unformed blood elements, causing edema. And polymorphonuclears, lymphocytes and perithelial cells invade the inflamed site. As a result of all these changes, the cellular environment reaches a state of turmoil.



*Phase-contrast microscopy showing mast cell before injury.*

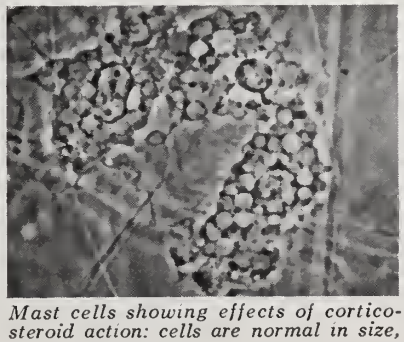


*Mast cell (after injury) has broken up and released cytotoxins.*

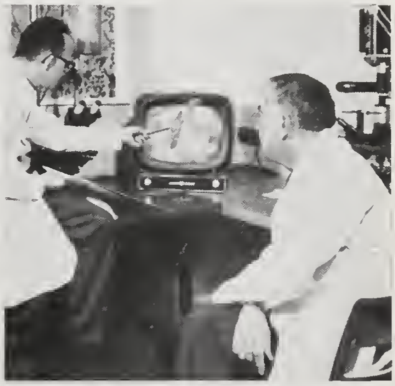
## How corticosteroids change the picture

Corticosteroids appear to virtually stop the abnormal cellular activity that constitutes the inflammatory reaction. This permits the body's natural resources to clear up the inflamed area and repair the damaged tissue. This interpretation is supported by the fact that when the injurious gelatin solution is injected simultaneously with a corticosteroid – Synalar (fluocinolone acetonide) – the inflammatory pattern simply does not develop.

*Fibroblast in high state of activity, much distorted.*



*Mast cells showing effects of corticosteroid action: cells are normal in size, shape and activity.*



In summarizing his study Doctor Dougherty states: "...we also feel this work may explain why one corticosteroid helps a patient more rapidly and effectively than another. If it does, it is because one corticosteroid is the fastest, most effective inhibitor of the series of inflammatory events at the tissue level."

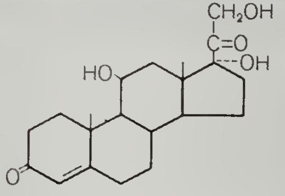
---

**A New View of Corticosteroid Action in Inflammatory Dermatoses*, a film based on this study, is now available from your Syntex representative.

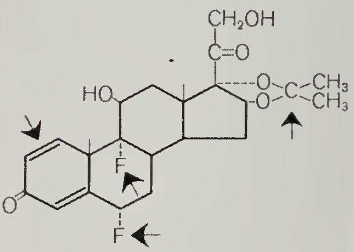
*See last page for contraindications, precautions, side effects and dosage*

# How advances in chemical design have achieved greater steroid potency

The chemical modification of corticosteroid molecules from the advent of hydrocortisone to the development of Synalar (fluocinolone acetonide) is a prime example of how biochemists can "design" to increase therapeutic activity and minimize undesirable side actions. Below, for example, we see the important changes that were made in reference to the hydrocortisone molecule to produce fluocinolone acetonide, one of the most active of all topical corticosteroids. As a result, a 0.01% preparation of Synalar (fluocinolone acetonide) has been reported to do the work of a 1% hydrocortisone product containing 100 times more cortiscosteroid. And it can often do it more effectively.



**Hydrocortisone**

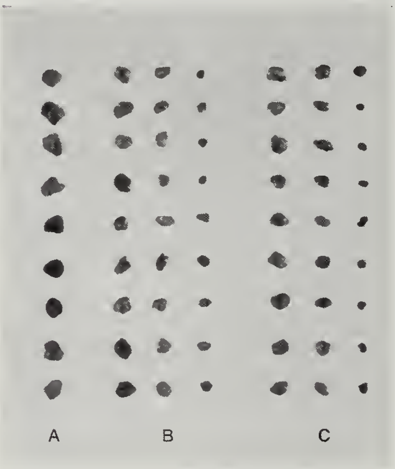


**Fluocinolone Acetonide (Synalar)**

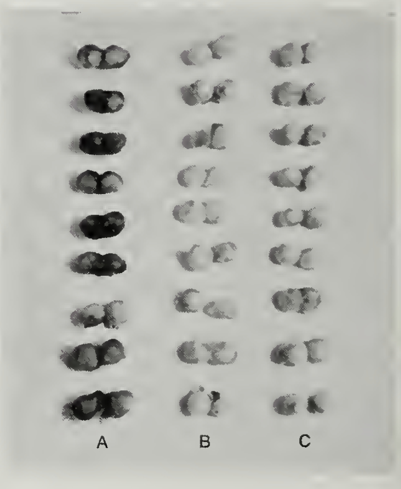
- ☐ *a double bond between carbons 1 and 2*
- ☐ *fluorine substitutions at both the 6-α, and the 9-α positions*
- ☐ *the addition of the acetonide at the 16-α, 17-α positions, thus providing one of the most potent topical corticosteroids available.*

### How bioassay tests are used to "predict" therapeutic potential

Biologic assays are another tool used by researchers to help establish the relative activity of corticosteroids. To date no single method of assaying corticosteroid activity has emerged as the ideal "yardstick" for predicting therapeutic potential. Taken together, however, these methods have proved useful. When such tests are run on various corticosteroids, a definite order of corticosteroid activity becomes evident. Compounds with the highest order of activity may be expected to merit clinical trial to establish their high therapeutic potential. When assayed by these methods, fluocinolone acetonide (Synalar) emerges as one of the most active topical corticosteroids, milligram for milligram, available for clinical application today.



THE THYMUS INVOLUTION ASSAY[1-4] is run on adrenalectomized rats. The sizes of the glands are measured, and the degree of involution caused by the steroid is determined as an indication of its potency. In the above photo, the comparative involution of thymus glands achieved with hydrocortisone and Synalar (fluocinolone acetonide) is shown. Untreated controls (A) show normal size. Group B – injected with 1, 2 and 4 mg. of hydrocortisone – show progressively smaller thymuses as does Group C – injected with fluocinolone acetonide – but with only 1/500th the dose of hydrocortisone.



THE ANTIGRANULOMA ASSAY[1-4] also utilizes adrenalectomized rats. Granulomas are induced by subcutaneous implantation of cotton pellets on either side of the thorax. The degree of granuloma inhibition achieved by a steroid reflects its potency. The above photo shows the inhibition of granuloma formation achieved with hydrocortisone and Synalar (fluocinolone acetonide). Untreated controls (A) show large, red granulomas adhering to the pellets. Group B, receiving hydrocortisone and Group C, receiving fluocinolone acetonide, show little, if any, granuloma formation. Fluocinolone acetonide produced the same effect as hydrocortisone with only 1/500th the dose. This assay, as well as the thymus involution assay, measures systemic rather than topical corticosteroid activity. Nevertheless, results by these methods correlate well with other assays and with the milligram potencies of topical steroids in current clinical use.

# Worldwide clinical experience confirms the predictable therapeutic potential of Synalar

It is particularly gratifying that the promise of the advanced chemical design and high order of bioassay activity of Synalar (fluocinolone acetonide) has been confirmed by widespread therapeutic application. Indeed, the impressive clinical response rate of Synalar has been documented in no fewer than 232 papers from 22 countries.

## Representative Clinical Results with Synalar*

### Efficacy Documented in over 4,000 Patients

| Condition | Number of Publications | Number of Patients | Significant Improvement† |
|---|---|---|---|
| Contact Dermatitis | 27 | 750 | 713 |
| Eczematous Dermatitis | 21 | 472 | 409 |
| Seborrheic Dermatitis | 18 | 442 | 426 |
| Atopic Dermatitis | 24 | 460 | 426 |
| Psoriasis | 36 | 1,699 | 1,510 |
| Neurodermatitis | 18 | 351 | 324 |
| Total | 144 | 4,174 | 3,808 |

*Complete bibliography on request.

†Expressed by the authors as excellent, very good, good, complete remission of inflammation, etc.

PRESCRIBING INFORMATION

*For initiation of therapy:* Cream 0.025%, 5 and 15 Gm. tubes, 425 Gm. jars; *for emollient effect:* Ointment 0.025%, 15 Gm. tubes; *for maintenance therapy:* Cream 0.01%, 15 and 45 Gm. tubes, 120 Gm. jars; *for intertriginous or hairy sites:* Solution 0.01%, 20 cc. and 60 cc. plastic squeeze bottles; *for infected inflammatory dermatoses:* Neo-Synalar® Cream (0.025% fluocinolone acetonide, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes. CONTRAINDICATIONS: Tuberculous, fungal, and most viral lesions of the skin, (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. PRECAUTIONS: Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. When severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. SIDE EFFECTS: Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. The neomycin in Neo-Synalar Cream rarely produces allergic reactions.

REFERENCES: 1. Lerner, L. J., Bianchi, A., Turkheimer, A. R., Singer, F. M., and Borman, A.: Anti-inflammatory steroids: potency, duration and modification of activities. Ann NY Acad Sci 116:1071 (Aug. 27) 1964. 2. Idem: Comparison of anti-granuloma, thymolytic and glucocorticoid activities of anti-inflammatory steroids. Proc Soc Exp Biol Med 116:385 (June) 1964. 3. Ringler, A.: Activities of adrenocorticosteroids in experimental animals and man, in Dorfman, R. I.: Methods of hormone research, New York, Academic Press, 1964. vol. III. pp. 234-280. 4. Gubersky, V. R.: To be published.

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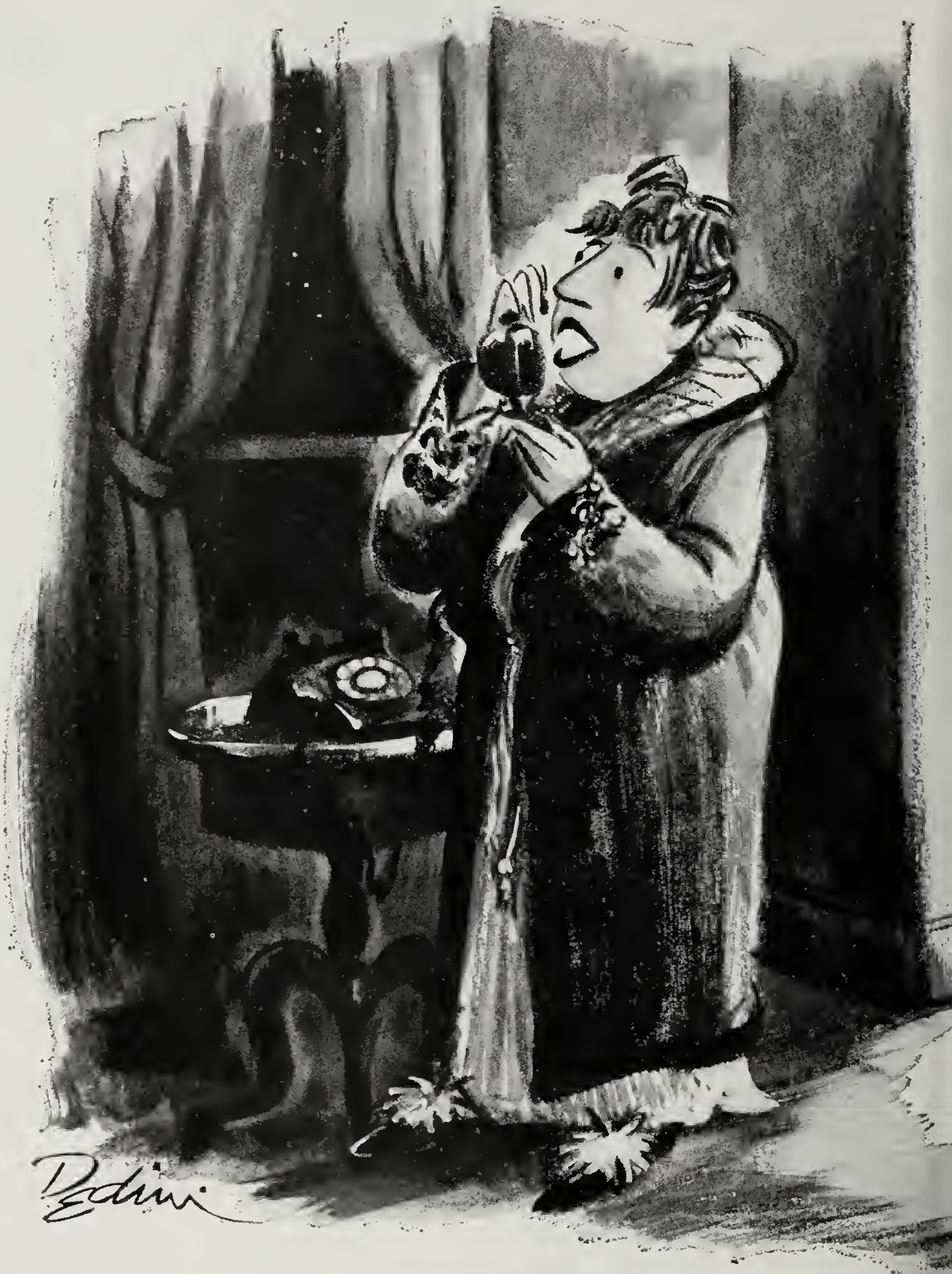

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in the control of pain

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pentazocine
(as lactate)

a potent injectable non-narcotic—
may be used in place of morphine
and other narcotic analgesics

# A breakthrough in the control of pain

# Talwin®

brand of
**pentazocine**
(as lactate)

**a potent injectable non-narcotic— may be used in place of morphine and other narcotic analgesics**

## Talwin 30 mg. relieves pain usually as quickly and effectively as morphine 10 mg.[*]

**whatever the intensity of the pain**

**whatever the cause of the pain**

**whatever the site[†] of the pain**

**whatever the chronicity of the pain**

**whatever the age[††] of the patient**

**without the liability of narcotics**

**without the development of tolerance on prolonged use**

**with less risk of severe respiratory depression than with morphine**

**with less constipation**

**with less urinary retention**

Clinical experience of more than 150 investigators with over 12,000 patients given varying dosages of Talwin shows that this potent injectable analgesic is not a narcotic.

Talwin has less risk of severe respiratory depression, urinary retention, and constipation than morphine—a great boon for postsurgical patients.

Talwin produces less nausea, vomiting and diaphoresis than meperidine.

Constipation and urinary retention are seldom a problem with Talwin.

Very rarely do hallucinations or disorientation occur (0.1% each).

No significant hepatic, renal, hematopoietic or neurologic disturbances have been reported.

Talwin is well tolerated even by the aged or very ill patients.

Used during active labor, its tolerance by the mother and newborn is comparable to meperidine's. As with all new drugs, Talwin should be used with caution in pregnant women and in women delivering premature infants.

Tolerance to the analgesic effect of Talwin has not developed with prolonged use.

Talwin gives significant relief of pain in from 15 to 20 minutes following I.M. or S.C. injection.

Talwin relieves pain usually for 3 hours or longer with a single injection; however, the duration may sometimes be less than with morphine.

## 86 per cent of medical and surgical patients obtained excellent to good relief with Talwin 30 mg. administered

---

[*] Its duration of action may sometimes be less than that of morphine.

[†] Should not be used for patients with increased intracranial pressure, head injury or pathologic brain conditions.

[††] Until sufficient experience is gained, Talwin should not be administered to children under 12 years of

# Talwin
## brand of pentazocine (as lactate)
# used for pain of all types

## Talwin has a wide range of usefulness in surgery

| Types of surgical use | Number of patients | Efficacy % Exc. | % Good | Exc. + Good | % Fair | % Poor |
|---|---|---|---|---|---|---|
| • Preoperative | 118 | 31 | 52 | 83% | 15 | 2 |
| • Postoperative | 914 | 58 | 28 | 86% | 8 | 6 |
| • Pre- and postoperative | 12 | 75 | 17 | 92% | 0 | 8 |
| • Minor surgery | 33 | 30 | 39 | 69% | 0 | 31* |
| • Traumatic | 14 | 64 | 29 | 93% | 7 | 0 |
| • Dental | 33 | 67 | 24 | 91% | 3 | 6 |

Total patients............1124

Efficacy of 30 mg. Talwin I.M. and S.C. as related to types of surgical use in a cooperative study

Data in files of Department of Medical Research, Winthrop Laboratories.

*High incidence of poor results in minor surgery is due primarily to one study involving change of burn dressings in children; 9 of 19 patients obtained poor results with dose used.

## Talwin relieves all types of pain in acute and chronic medical disorders

| Type of medical pain | Number of patients | Percentage of relief: Excellent | Good | Exc. + Good | Fair | Poor |
|---|---|---|---|---|---|---|
| • Malignancy, pain in | 161 | 44 | 37 | 81% | 8 | 11 |
| • Orthopedic; see also "Arthritis" | 111 | 53 | 38 | 91% | 5 | 4 |
| • Cardiovascular pain; see also "Miscellaneous medical" | 96 | 59 | 27 | 86% | 6 | 7 |
| • Genitourinary pain | 83 | 42 | 33 | 75% | 16 | 10 |
| • Arthritis | 76 | 33 | 51 | 84% | 12 | 4 |
| • Gynecologic pain | 35 | 57 | 34 | 91% | 6 | 3 |
| • Cephalalgia | 21 | 45 | 41 | 86% | 9 | 5 |
| • Gastrointestinal pain | 19 | 89 | 5 | 94% | 0 | 5 |
| • Chest, including<br>• Pleurisy<br>• Pulmonary embolism and infarct<br>• Lung abscess | 12 | 83 | 17 | 100% | 0 | 0 |
| • Miscellaneous medical, including<br>• Peripheral vascular disease<br>• Thrombophlebitis<br>• Cervical root pain<br>• Facial neuralgia<br>• Syringomyelia<br>• Burns | 108 | 50 | 39 | 89% | 9 | 2 |

Total patients............722

Efficacy of 30 mg. Talwin I.M. and S.C. as related to types of medical pain in a cooperative study

Data in files of Department of Medical Research, Winthrop Laboratories.

See next page for additional product information

## Talwin relieves pain as quickly as morphine

A comparison of Talwin 30 mg. and morphine 10 mg. I.M. in controlling postoperative pain*

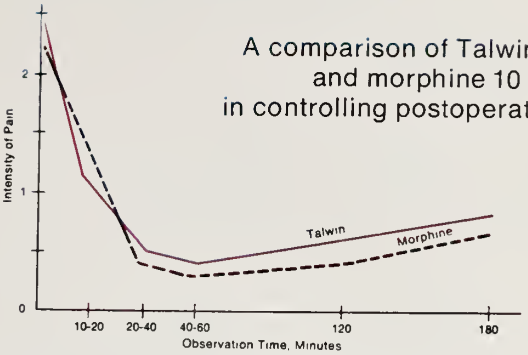


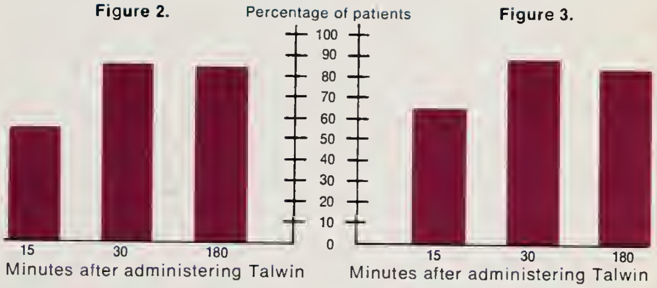
**Figure 1.**

Talwin 30 mg. proved equivalent to morphine 10 mg. in overall analgesic efficacy. During the early post-medication period (up to 40 minutes after drug injection), Talwin was superior in effect to morphine.

After observation periods ranging from 40 to 180 minutes there was no difference between the drugs in their effect on intensity. There were 141 and 119 complete patient records for Talwin and morphine, respectively, in this double-blind study. Other clinical investigators, studying duration, state that relief with Talwin may be obtained for up to three hours or longer, a period sometimes less than morphine's.

## Talwin is as effective for severe pain (Fig. 2) as for moderate pain (Fig. 3)

**Figure 2.** **Figure 3.**



Per cent excellent to good relief of severe pain obtained with 30 mg. Talwin in 218 postoperative patients

Per cent excellent to good relief of moderate pain obtained with 30 mg. Talwin in 203 postoperative patients

## Talwin does not require a narcotics prescription or narcotics records

The World Health Organization Expert Committee on Dependence-Producing Drugs concluded that "...there was no need at this time for narcotics control of pentazocine [Talwin] internationally or nationally."‡

---

*Storer, E. H.: Data in the files of the Sterling-Winthrop Research Institute.

†Cooperative study, data in the files of the Department of Medical Research, Winthrop Laboratories.

‡*World Health Organization Technical Report Series*, No. 343, 1966, p. 6.

# A breakthrough in the control of pain

# Talwin®

brand of

# pentazocine

(as lactate)

## a potent injectable non-narcotic—may be used in place of morphine and other narcotic analgesics

**Contraindications:** *Increased Intracranial Pressure, Head Injury, or Pathologic Brain Conditions in which clouding of sensorium is undesirable.* Talwin (brand of pentazocine) should not be administered in these cases, since drug-induced sedation, dizziness, nausea, or respiratory depression could be misleading.

**Precautions:** *Pregnancy.* No teratogenic or embryotoxic effects attributable to the use of Talwin have been seen in extensive reproductive studies in animals; however, like all new drugs, Talwin should be given with caution to pregnant women. A large number of patients in labor have received the drug with no adverse reactions other than those that occur with commonly used strong analgesics. However, as with other strong analgesics, Talwin should be used with caution in women delivering premature infants.

*Ambulatory Patients.* Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

*Certain Respiratory Conditions.* The possibility that Talwin (brand of pentazocine) may cause respiratory depression should be considered in treatment of patients with bronchial asthma. Talwin should be administered only with caution and in low dosage to patients with respiratory depression (e.g., from other medication, uremia, or severe infection), obstructive respiratory conditions, or cyanosis.

*Patients Dependent on Narcotics.* Because Talwin is a narcotic-antagonist, patients dependent on narcotics and receiving Talwin may occasionally experience certain withdrawal symptoms. Talwin should be given with special caution to such patients. It has been observed that some patients previously given narcotic-analgesics for one month or longer had mild withdrawal symptoms when the drug was replaced with the analgesic, Talwin. After a short period of adjustment the subjects were usually able and willing to continue taking Talwin, and relief of pain was satisfactory.

*Nonaddicted Patients Receiving Narcotics.* Symptoms believed to be indicative of antagonism to the opiate may be observed rarely with administration of Talwin to patients receiving opiates for a short time. Intolerance or untoward reactions are seldom observed after administration of Talwin to patients who have received single doses or who have had limited exposure to narcotics.

*Impaired Renal or Hepatic Function.* Although laboratory tests have not indicated that Talwin (brand of pentazocine) causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment. Extensive liver disease appears to predispose to greater side effects (e.g., marked apprehension, anxiety, dizziness, sleepiness) from the usual clinical dose, and may be the result of decreased metabolism of the drug by the liver.

*Myocardial Infarction.* As with all drugs, Talwin (brand of pentazocine) should be used with caution in patients with myocardial infarction who have nausea or vomiting.

*Biliary Surgery.* Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

**Adverse Effects:** Talwin is relatively free from the undesirable side effects associated with morphine, such as constipation, urinary retention, or severe respiratory depression. Furthermore, Talwin produces less nausea, vomiting, and diaphoresis than meperidine.

In over 12,000 patients who received Talwin intramuscularly, subcutaneously, or intravenously, nausea, the most frequent adverse effect, occurred in approximately 5.0 per cent. In decreasing order of occurrence were vertigo, dizziness or lightheadedness; vomiting; and euphoria. Respiratory depression was reported as an adverse reaction in 1.0 per cent.

The incidence of each of the other adverse effects was well below 1.0 per cent: constipation, circulatory depression, diaphoresis, urinary retention, alteration in mood (nervousness, apprehension, depression, floating feeling), hypertension, sting on injection, headache, dry mouth, flushed skin including plethora, altered uterine contractions during labor, dermatitis including pruritus, dreams, paresthesia, and dyspnea occurred rarely after administration of Talwin (brand of pentazocine). Furthermore, each of the following adverse reactions occurred in less than 0.1 per cent: tachycardia, visual disturbance (blurred vision, diplopia and nystagmus), hallucinations, disorientation, weakness or faintness, muscle tremor, chills, allergic reactions including edema of the face, taste alteration, insomnia, diarrhea, cramps, and miosis; laryngospasm in one patient.

Talwin has not produced severe respiratory embarrassment in adults (never apnea), even with large amounts. A small number of newborn infants whose mothers received Talwin during labor had transient apnea. The incidence of temporary diminution in the rate or strength of uterine contractions is low after administration of Talwin, similar to that following meperidine hydrochloride. (In reporting no interference with normal labor in patients receiving Talwin, one investigator further stated that the drug may increase uterine activity.) Generally, no significant fetal heart rate change occurs.

Laboratory tests of blood and of liver and kidney functions have revealed no significant abnormalities. A minimum and probably insignificant increase in the per cent of eosinophils in peripheral blood counts and bone marrow occurred occasionally.

Talwin is well tolerated by patients with diabetes mellitus, and no changes in insulin requirements have been observed.

**Dosage and Administration:** *Adults, Excluding Patients in Labor.* Average recommended single parenteral dose is 30 mg., by intramuscular, subcutaneous, or intravenous route; may be repeated every three to four hours. Pain has been relieved in most patients with not more than three doses daily. Infrequently, selected patients have received single doses as high as 60 mg.

*Patients in Labor.* A single, intramuscular 30 mg. dose has been most commonly administered. An intravenous 20 mg. dose has given adequate pain relief to some patients in labor when contractions become regular, and this dose may be given two or three times at two- to three-hour intervals, as needed.

*Children Under 12 Years of Age.* Since clinical experience in children under twelve years of age is limited, the use of Talwin (brand of pentazocine) in this age group is not recommended.

*Duration of Therapy.* Patients with chronic pain who received Talwin for prolonged periods (e.g., over 300 days) experienced no withdrawal symptoms even when administration was stopped abruptly; furthermore, there was no tolerance to the analgesic effect.

*CAUTION.* Talwin should not be mixed in the same syringe with soluble barbiturates because precipitation will occur.

*Treatment of Overdosage or Respiratory Depression.* Talwin has not produced apnea or severe respiratory embarrassment in adults, even in large doses. Occasionally, however, moderate respiratory depression may occur. Means of maintaining proper oxygenation should be available in case of overdosage or respiratory depression, and methylphenidate (Ritalin®) should be administered parenterally. The usual narcotic-antagonists, such as nalorphine, are not effective respiratory stimulants for depression due to Talwin.

**How Supplied: Ampuls of 1 ml., containing Talwin® (pentazocine) as lactate equivalent to 30 mg. base** and 2.8 mg. sodium chloride, in Water for Injection. **Boxes of 10, 25, and 100.**

**Multiple dose vials of 10 ml., each 1 ml. containing Talwin® (pentazocine) as lactate equivalent to 30 mg. base,** 2 mg. acetone sodium bisulfite, 1.5 mg. sodium chloride, and 1 mg. methylparaben as preservative, in Water for Injection. **Boxes of 1.**

The pH of Talwin solutions is adjusted between 4 and 5 with lactic acid and sodium hydroxide.

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PRINTED IN U.S.A. ISSUED AUGUST, 1967 (1035M)

# BOOK REVIEWS

**Current Concepts in Ophthalmology.** Bernard Becker, M.D., and Robert C. Drews, M.D. Price, $17.25. Pp. 265, with 127 illustrations. St. Louis: Mosby, 1967.

A quotation from the editors' preface will serve to outline the general purpose and content of this very informative volume: "This book is a compilation of selected topics representing some of the current clinical work and interests of the staff of The Department of Ophthalmology, Washington University School of Medicine. . . . The editors intended a probing and questioning analysis by the several authors of areas involved in the most interesting current concepts in ophthalmology."

For the ophthalmologist performing, or intending to perform, office tonography, the 4 chapters by Dr. Drews on this subject should be invaluable; his discussion ranges from the selection of tonographic equipment to the interpretation of difficult tonograms.

The chapter by Dr. Becker dealing with the effects of topical corticosteroids on the intraocular pressure in various population groups and the possible relationship of these effects to the hereditary transmission of glaucoma is very timely. It summarizes and brings together much of the material on this subject which has been dispersed throughout the ophthalmic literature in recent years.

In general, although the subject matter is slanted toward glaucoma (7 of 21 chapters), a wide variety of subjects is presented in a concise, interesting form, making this a very readable and worthwhile book.

Don R. Johnson, M.D.

**Current Therapy 1967. Latest Approved Methods of Treatment for the Practicing Physician.** Edited by Howard F. Conn, M.D. with 12 Consulting Editors and 332 Contributors. Price, $13.00. Pp. 844. Philadelphia: Saunders, 1967.

This nineteenth annual edition is written by 332 authors. The stated purpose of the book remains the same: providing up-to-date information on the treatment of commonly encountered diseases. The volume is obviously intended for those practicing internal medicine. It includes a handy reference to potential chemical poisons and their treatment, as well as a list of poisonous ingredients in household products adpated from *American Druggist.* Normal laboratory values, height and weight tables, and a brief discussion of units of measurement are included.

The practicing physician who becomes aware of his need to look up the "latest approved method" of managing a disease will usually need to bring himself up to date regarding other aspects of that disease in order to achieve the confidence required for intelligent management. The editors and authors recognize this need by their introductory notes on classification, pathogenesis, and differential diagnosis. However, this ned is well served by current editions of the various excellent textbooks of internal medicine, copies of which should be on every physician's shelf. This lack may detract somewhat from this book's usefulness but it would be invaluable as a ready reference, especially in hospital wards and emergency rooms.

The selection of contributors is generally of the highest caliber, predominantly composed of experienced physicians with a practical approach.

Despite the editor's explanations regarding the term "method of" preceding authors' names, it would be well to avoid erroneous implications by omitting this redundancy in future editions. Similarly, the chapters on the psychotherapy of mental diseases do not belong in this volume. This is not where one learns how to treat schizophrenia.

Garo S. Matossian, M.D.

**The Neuroses.** Henry P. Laughlin, M.D. Price, $25.00. Pp. 1076. Washington: Butterworths, 1967 (distributed by Appleton-Century-Crofts).

This book, according to the preface, was written "for everyone who is concerned with emotions, motivation and behavior," which is a very fair statement with regard to both its content and its organization; together they afford maximum intelligibility and ease of locating facts.

It is a predominantly practical book, and theoretical discussions are related to clinical data by means of numerous examples illustrating symptoms and diagnostic categories. Although his dynamic orientation is obvious, Dr. Laughlin has been careful always to write understandably and never to indulge in the kind of obscure pedantry which has sometimes earned for psychiatrists a reputation for being more mystical than scientific. The author points out, as well as anyone has ever done, the centrality of anxiety in psychiatric illness and the purpose of symptoms and character defenses as methods of avoiding anxiety. The text then proceeds in orderly fashion to a consideration of the various types of neuroses and character defenses, including their historical background, diagnosis, symptomatology, psychodynamics and treatment. One category which seems to be original with Dr. Laughlin is that of the soterial reactions, defined as the opposite of phobias, wherein one derives security and comfort not only from external objects, such as charms, amulets, etc., but also from medicines, foods, and such common objects.

It is also a well organized book. Not only are there an adequate table of contents and index, but an exhaustive outline at the beginning of each chapter, a useful bibliography and review questions at the end of each chapter, and a glossary at the end of the book. Important definitions are always italicized, and the author has included 48 tables, bringing together groups of related facts, such as, to name 2 titles, Types of Dissociation and Determinants in Symptom Choice in Conversions.

I differed with Dr. Laughlin with regard to his sub-

(*Continued on page 54*)

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## Book Reviews

(*Continued from page 53*)

stitution of *hygeiaphrontis* for *hypochondriasis* (granted that the former term is etymologically correct) because the definition of the latter term is well known and its use causes no confusion. Moreover, I was not happy over his enunciation of a number of principles which he referred to further on in the text by their abbreviations. However, these are minor criticisms of a well organized, eminently intelligible treatment of the subject which should be of great value to students in the behavioral sciences, interns, and psychiatric residents as well as a useful review for practicing psychiatrists.

Robert J. Brown III, M.D.

**Handbook of Orthopaedic Surgery,** 7th ed. Alfred R. Shands, Jr., M.D., F.A.C.S., and R. Beverly Raney, Sr., M.D., F.A.C.S., with the collaboration of H. Robert Brashear, M.D., F.A.C.S. Price, $12.00. Pp. 572, with 269 illustrations. St. Louis: Mosby, 1967.

The seventh edition of this comprehensive text is composed of 22 chapters dealing with all phases of orthopedic surgery, with new sections on avascular necrosis of the femoral head, paralytic affectations, and the disease of ochronosis and chondrocalcinosis.

There is a generous sprinkling of pediatric orthopedics throughout the volume, reflecting the vast knowledge of Dr. Alfred R. Shands, Jr.

I was most impressed by the inclusion in this volume of many conditions quite commonly seen in the general practice of orthopedics which do not appear in many of the other orthopedic texts.

The illustrations and reproductions of X-ray pictures are excellent and should be very useful to students and general practitioners.

This volume should be part of the library of all those who practice general medicine as well as the students, residents, and practitioners of orthopedic surgery.

Ernest D. Martin, M.D.

**Ciba Foundation Symposium: Principles of Biomolecular Organization.** Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Maeve O'Connor, B.A. Price, $15.00. Pp. 491, with 141 illustrations. Boston: Little, 1966.

This book of 491 pages is the result of a Symposium on the Principles of Biomolecular Organization held in June 1965 under the sponsorship of the Ciba Foundation. The contributors to this volume were 29 research investigators from various parts of the world. After each presentation there is a valuable discussion of the subject by members of the panel. Because of the highly theoretical and sometimes philosophical consideration of submolecular biology, the reader finds some difficulty in digesting the subject matter. However, some chapters, e.g., Control Mechanisms in Bacteriophage Mor-

(*Continued on page 55*)

## Book Reviews

*(Continued from page 54)*

phopoiesis and The Design of Contractile Systems, are well written and illustrated.

This book will have an appeal limited to those interested in cellular biology, namely, anatomists, virologists, and physiologists. Some chapters, such as Stabilizing Interactions in Globular Proteins, by Kendrew and Watson, and Minimum Energy Conformations of Biological Polymers, by Liquori, would be interesting to the biochemist.

VERNON E. MARTENS, M.D.

**Ciba Foundation Study Group No. 25. Mongolism.** In Commemoration of Dr. John Langdon Haydon Down. Edited by G. E. W. WOLSTENHOLME, O.B.E., M.A., F.R.C.P., F.I.BIOL., AND RUTH PORTER, M.R.C.P. Price, $3.50. Pp. 99, with 23 illustrations. Boston: Little, 1967.

Although it was described over a hundred years ago, relatively little was understood about the causation and pathogenesis of mongolism (Down's syndrome) until the discovery in 1959 of an extra chromosome in the cells of affected individuals. Considerable progress has been made since then in many areas. Several types of anomalies of chromosome 21 that lead to mongolism have been defined, and factors that may predispose to their occurrence have been investigated. Abnormalities of hand- and footprint patterns have been intensively analyzed and have provided useful clinical tools. Studies of enzymes in cells of blood and other tissues have revealed abnormalities in the activities of several enzymes. While these abnormalities do not appear to be the primary effects of the extra chromosomal material, they do indicate the types of biochemical manifestations that chromosomal aberrations may have. Most recently, a possible therapeutic approach to some of the manifestations of the disorder, if not to their underlying causes, has been described.

All of these subjects but the last are touched upon in the small volume on "Mongolism" issued as a report of the deliberations of a Ciba Foundation Study Group which met in May 1966 to commemorate the 100th anniversary of Dr. John Langdon Haydon Down's description of the syndrome. This collection of a historical introduction, 7 formal papers, and attendant discussion has the virtues of brevity, inexpensiveness, relative rapidity of appearance, and attractiveness of format. However, the articles, while interesting in themselves, are quite narrow in scope, and no attempt was made to present a coherent picture of the current state of knowledge. Important information often appears only in the fine print of the discussions, and a prior familiarity with the subject is usually assumed. This book cannot, therefore, be recommended to the interested but uninitiated reader, and it must be judged less successful than its big cousins, The Ciba Symposia, after which it is patterned.

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| Triaminic® | 50 mg. |
| (phenylpropanolamine hydrochloride 25 mg., pheniramine maleate 12.5 mg., pyrilamine maleate 12.5 mg.) | |
| Dextromethorphan hydrobromide | 30 mg. |
| Terpin hydrate | 180 mg. |
| Acetaminophen | 325 mg. |

Dosage: Adults—1 tablet, swallowed whole to preserve timed-release feature, in morning, midafternoon and at bedtime. Side effects: Occasional drowsiness, blurred vision, cardiac palpitations, flushing, dizziness, nervousness or gastrointestinal upsets. Precautions: The patient should be advised not to drive a car or operate dangerous machinery if drowsiness occurs. Use with caution in patients with hypertension, heart disease, diabetes or thyrotoxicosis.

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Deserpidine
Methyclothiazide
200
180
160
140
120
100
80

# Consider starting your hypertensives on this basic thiazide

ABBOTT

## A single daily dose of Enduron provides sodium excretion around the clock

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Use Enduron as an ideal starting therapy in mild hypertension. Use it too, as a basic therapeutic building block with which other agents can be joined, for managing your more resistant hypertensives.

ENDURON
ENDURON
METHYCLOTHIAZIDE
Methyclothiazide

*Once a day, every day*

**ENDURON®**
**METHYCLOTHIAZIDE**

| DAILY DOSAGE RANGE | Minimum | Usual | Intermediate | Maximum |
|---|---|---|---|---|
| | <br>2.5 mg. tablet | <br>5 mg. tablet | <br>7.5 mg. | <br>10 mg. |

*See Brief Summary on final page of advertisement.*

# To build added response, shift to Enduronyl

ABBOTT

## The deserpidine component adds enhanced antihypertensive activity

The rauwolfia component of Enduronyl is deserpidine (Harmonyl®), a purified crystalline alkaloid supplied only by Abbott. It augments Enduron with its own antihypertensive and tranquilizing action.

Thus the combined clinical effect of these two therapeutic building blocks in Enduronyl is greater than can ordinarily be achieved with either alone.

To add flexibility, Enduronyl comes in two strengths: regular and Forte. Both provide 5 mg. of Enduron. The variation is where most helpful: in the deserpidine. The tablets are scored, and give a surprisingly wide and economical choice of once-a-day doses (see below).

Choose Enduronyl for your patients in the broad range of mild to moderate hypertension. Patient acceptance is excellent!

Deserpidine
Methyclothiazide

*Once a day, every day*

**ENDURONYL®**

METHYCLOTHIAZIDE 5 MG. WITH DESERPIDINE 0.25 MG.

**ENDURONYL FORTE**

METHYCLOTHIAZIDE 5 MG. WITH DESERPIDINE 0.5 MG.

| | Minimum | Usual | Intermediate | Maximum |
|---|---|---|---|---|
| DAILY DOSAGE RANGE | <br>2.5 mg. methyclothiazide<br>0.125 mg. deserpidine | <br>5 mg. methyclothiazide<br>0.25 mg. deserpidine | <br>7.5 mg. methyclothiazide<br>0.375 mg. deserpidine | <br>10 mg. methyclothiazide<br>0.5 mg. deserpidine |
| DAILY DOSAGE RANGE | <br>2.5 mg. methyclothiazide<br>0.25 mg. deserpidine | <br>5 mg. methyclothiazide<br>0.5 mg. deserpidine | <br>7.5 mg. methyclothiazide<br>0.75 mg. deserpidine | <br>10 mg. methyclothiazide<br>1 mg. deserpidine |

*See Brief Summary on final page of advertisement.*

707075-R

# ENDURON® | ENDURONYL®

**METHYCLOTHIAZIDE**

Each tablet contains
Methyclothiazide 5 mg. with
Deserpidine 0.25 mg. or 0.5 mg.

*Indications:* Enduron is used to control edema and mild to moderate hypertension; also used with other drugs for hypertension. Enduronyl is used in mild to moderately severe hypertension; when used with Enduronyl, more potent agents can be given at reduced dosage to minimize undesirable side effects.

*Contraindications:* Neither Enduron nor Enduronyl should be used in severe renal disease (except nephrosis) or shutdown; in severe hepatic disease or impending hepatic coma; in patients sensitive to thiazides. Hepatic coma has been reported as a result of hypokalemia in patients receiving thiazides.

Enduronyl is contraindicated in patients with severe mental depression and suicidal tendencies, active peptic ulcer, or ulcerative colitis.

*Warnings:* Consider possible sensitivity reactions in patients with a history of allergy or asthma. If added potassium intake is indicated, dietary supplementation is recommended. Enteric-coated potassium tablets should be reserved for cautious use only when adequate dietary supplementation is not practical because those tablets may induce serious or fatal small bowel lesions consisting of stenosis with or without ulceration. These small bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs.

*Precautions:* Use thiazides with caution in severe renal dysfunction, impaired hepatic function, or progressive liver disease. In surgical patients, thiazides may reduce the response to vasopressors and increase the response to tubocurarine. Use thiazides with caution in pregnancy (bone marrow depression, thrombocytopenia, or altered carbohydrate metabolism have been reported in certain newborn infants). Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. Antihypertensive response may be enhanced following sympathectomy.

Use Enduronyl with caution in patients with a history of peptic ulcer, as rauwolfias may increase gastric secretion. Discontinue at the first sign of mental depression. Rauwolfia alkaloids may increase hypotensive effects of surgery or anesthesia, and should be discontinued two weeks prior. They also lower the convulsive threshold and shorten seizure latency. In epilepsy, dosage adjustment of anticonvulsant medication may be necessary. Alcohol, barbiturates, or narcotics may potentiate action of deserpidine.

*Adverse Reactions:* During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). All patients should be observed for signs of hyponatremia ("low-salt" syndrome). Reported thiazide reactions include: anorexia, nausea, vomiting, diarrhea, headache, skin rash, dizziness, paresthesia, weakness, photosensitivity, jaundice, and pancreatitis.

Reported rauwolfia reactions include: nasal stuffiness, nausea, weight gain, diarrhea, aggravation of peptic ulcer, epistaxis, skin eruption, and reduction of libido and potency. Excessive drowsiness, fatigue, weakness, and nightmares may signal early signs of mental depression.

# EUTONYL® | EUTRON™

**PARGYLINE HYDROCHLORIDE**

Each tablet contains
Pargyline Hydrochloride 25 mg.
with Methyclothiazide 5 mg.

*Indications:* For treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. Not recommended for patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone. It is desirable to establish the dosage of Eutron by administering component drugs separately.

TM-Trademark.

*Contraindications:* Pheochromocytoma, advanced renal disease, increasing renal dysfunction, paranoid schizophrenia and hyperthyroidism. Hepatic coma has been reported as consequence of hypokalemia with thiazide therapy. Until further experience is gained not recommended for patients with malignant hypertension, children under 12, or pregnant patients.

Concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. 2 week interval should separate therapy and use of these agents.

Methyclothiazide is contraindicated in patients with known sensitivity to thiazides.

*Warnings:* Pargyline hydrochloride is a monoamine oxidase inhibitor. Warn patients against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When indicated, alcohol, narcotics (meperidine should be avoided), antihistamines, barbiturates, chloral hydrate, and other hypnotics, sedatives, tranquilizers, or caffeine, may be used cautiously in reduced dosage. In emergency surgery ¼ to ⅕ the usual dose of narcotics, analgesics, and other premedications should be used avoiding parenteral administration where possible. Carefully adjust dose of anesthetics to response of patient. Withdraw pargyline two weeks before elective surgery.

Warn patients about the possibility of postural hypotension. Those with angina or coronary artery disease should not increase physical activity with an improvement in well being. Pargyline may lower blood sugar.

Avoid use of enteric-coated potassium tablets, as these may induce serious or fatal small-bowel lesions consisting of stenosis with or without ulceration. These small-bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs. These products contain no added potassium salts and if added potassium intake is desired, dietary supplementation is recommended. Coated potassium tablets should be reserved for cautious use when adequate dietary supplementation is impractical. In patients with a history of allergy or asthma the possibility of sensitivity reactions should be considered.

*Precautions:* Measure blood pressure while patient is standing to determine antihypertensive effect. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Use with caution in patients with liver disease. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. With prolonged therapy, examine patients for change in color perception, visual fields and fundi. Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. In surgical patients thiazides may reduce response to vasopressors and increase response to tubocurarine.

*Adverse Reactions:* Pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extrapyramidal symptoms have been reported in a few patients with reduced cardiac reserve.

During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). Observe all patients for signs of hyponatremia ("low salt" syndrome).

Reported thiazide reactions also include anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, and pancreatitis. Nocturia has been observed with the combination.

709075R

ABBOTT

MEMO FROM . . .

to :

DR. "A"*
Administrator, Income Protection Plan,
Medical Society of the District of Columbia

# *"Thank you for relieving me of a financial burden"*

Dr. "A", Washington, D.C., was mighty thankful he had the Medical Society's Income Protection Plan when he was disabled recently by an accident.

Mutual of Omaha, underwriter of the plan, sent Dr. "A" a check for $2,562.60, paying him benefits under his Medical Society coverage as well as the supplementary coverage he has had with Mutual of Omaha since 1932.

All told, Mutual of Omaha has paid Dr. "A" a total of $8,003.38 in benefits since 1955. These checks, covering three separate disabilities, have helped him meet his financial obligations when he was unable to carry on his practice.

On each occasion Dr. "A" has been completely satisfied with the manner in which his applications for benefits have been handled and said so in a recent letter to Mutual of Omaha.

To put it in his own words: "I feel that my best friend in time of need has been Mutual of Omaha."

## Others Sing the Praises of Their Medical Society Protection Too:

### Dr. "B"*
Laurel, Maryland

Since purchasing his Medical Society Income Protection Plan in 1953, Dr. "B" has been disabled five times. He has received benefit checks totaling $1,199.91. Says Dr. "B": "I can truly state that I am very satisfied with my policy with Mutual of Omaha and wish to express my sincere thanks."

### Dr. "C"*
Washington, D. C.

When Dr. "C" received his benefit draft for $1,050.00 he commented that he was "most gratified to hear from Mutual of Omaha. Payment of sick benefits was made promptly, and was most appreciated at that time. I have nothing but praise for your organization and appreciate very much the privilege of holding a policy with you."

### Dr. "D"*
Glenn Dale, Maryland

After receiving benefits five times for a total of $628.54, Dr. "D" has this to say about his Mutual of Omaha coverage: "I would not hesitate to recommend your company to any of my friends, and can understand why Mutual of Omaha was selected to underwrite the Medical Society's group plan."

These people know from experience the importance of protecting their most valuable asset—*their ability to earn an income.* How about you? Is your income protected? If not, contact your Medical Society's Insurance Administrator today. He'll be happy to give you full details on the Medical Society's own Income Protection Plan, the same outstanding coverage that has provided so much financial security to these, your fellow members, in time of sickness or accident. It's the only plan specifically designed for Medical Society members by MUTUAL OF OMAHA, the greatest name in health insurance.

**Joseph E. Jones, Administrator**
**1666 Connecticut Avenue, N.W.**
**Washington, D. C. 20009**
**Tel. 483-3100**

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**MUTUAL OF OMAHA INSURANCE COMPANY**
**Life Insurance Affiliate: United of Omaha**
**Home Office: Omaha, Nebraska**

*Documented in the files of MUTUAL OF OMAHA

# Tears without grief

**Crying Spells – psychic tension with depressive symptoms?**

*"I don't know what's the matter with me lately...I cry and I cry... and I really don't know why I do."*

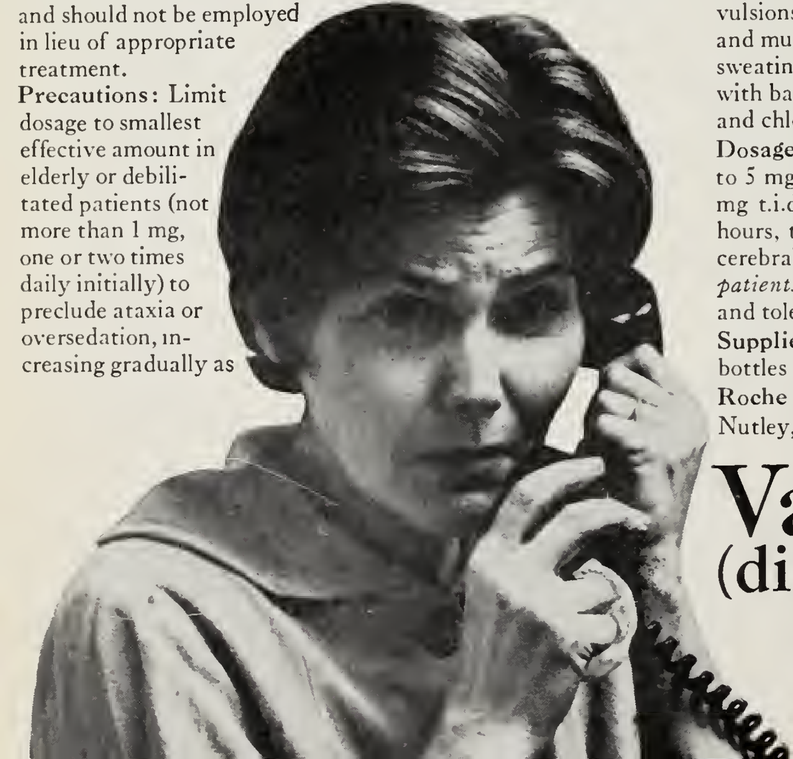
A woman often is not conscious of the real reasons for her crying spells or refuses to admit them to herself. On probing, you may find that frequent weeping, like insomnia or neurotic fatigue, often is an expression of psychic tension. She needs sympathy and reassurance, and perhaps a calming agent to help her over her crisis. Consider prescribing Valium (diazepam) for her. It usually reestablishes calmness promptly. Crying spells and other secondary depressive symptoms normally subside as the tension is relieved. Your patient then can cope more easily with stresses to which she is subjected. Valium (diazepam) is generally well tolerated, and on proper maintenance dosage usually does not impair mental acuity or ability to function. If side effects such as ataxia and drowsiness occur, they usually disappear with dosage adjustment.

Before prescribing, please consult complete product information, a summary of which follows:

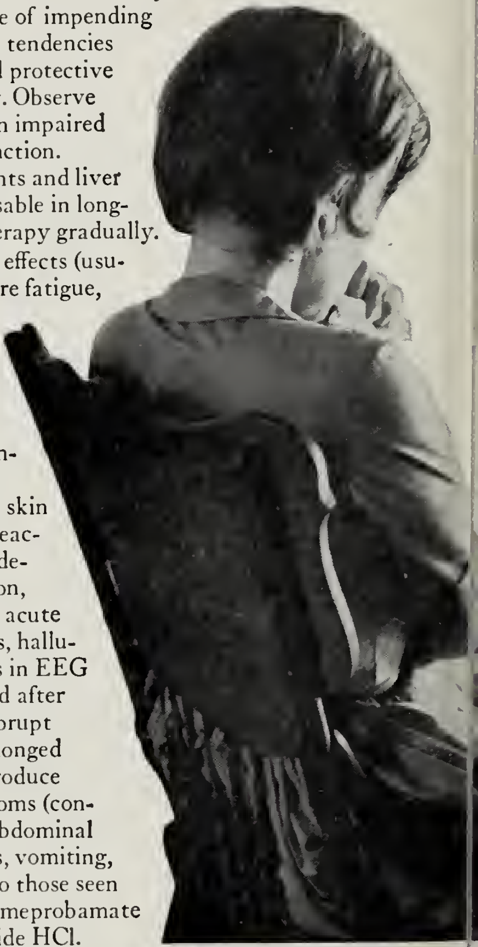
**Contraindications:** Infants, patients with history of convulsive disorders, glaucoma or known hypersensitivity to drug.

**Warning:** Not of value in the treatment of psychotic patients, and should not be employed in lieu of appropriate treatment.

**Precautions:** Limit dosage to smallest effective amount in elderly or debilitated patients (not more than 1 mg, one or two times daily initially) to preclude ataxia or oversedation, increasing gradually as needed or tolerated. As is true of all CNS-acting drugs, until correct maintenance dosage is established, advise patients against possibly hazardous procedures requiring complete mental alertness or physical coordination. Driving during therapy not recommended. In general, concurrent use with other psychotropic agents is not recommended. If such combination therapy is used, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium (diazepam), such as phenothiazines, barbiturates, MAO inhibitors and other antidepressants. Advise patients against simultaneous ingestion of alcohol or other CNS depressants. Safe use in pregnancy not established. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Observe usual precautions in impaired renal or hepatic function. Periodic blood counts and liver function tests advisable in long-term use. Cease therapy gradually.



**Side Effects:** Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances, acute hyperexcited states, hallucinations); changes in EEG patterns during and after drug treatment. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms (convulsions, tremor, abdominal and muscle cramps, vomiting, sweating) similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.



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**Medical Genetics**
Mihaly Bartalos, M.D.

**Massive Gastrointestinal Hemorrhage**
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**Visualization of Pelvic Lymphatics**
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**Thalassemia Syndromes and Hemoglobinopathies**
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**Trends in Neonatal Mortality**
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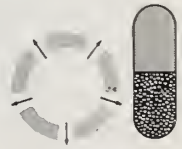

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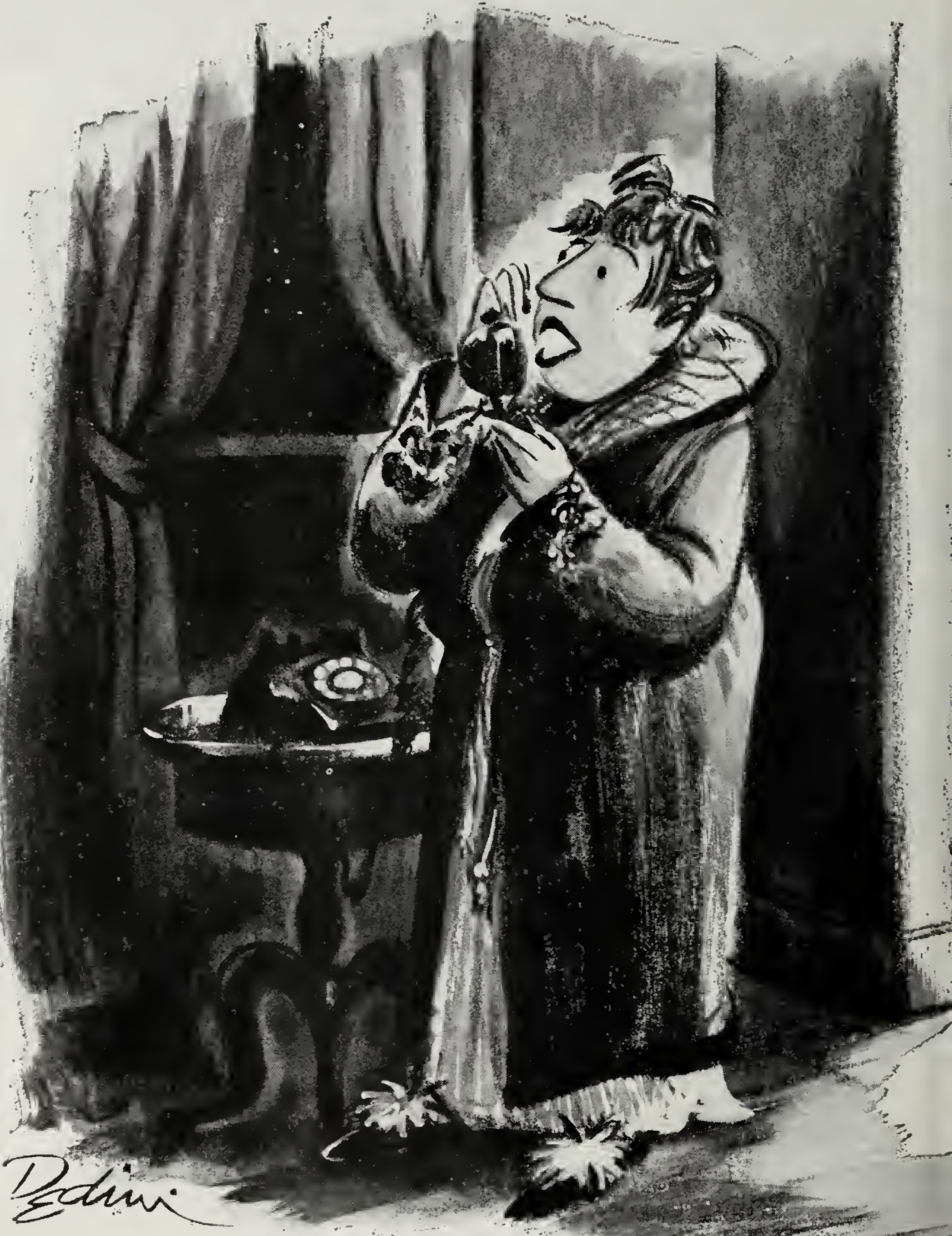

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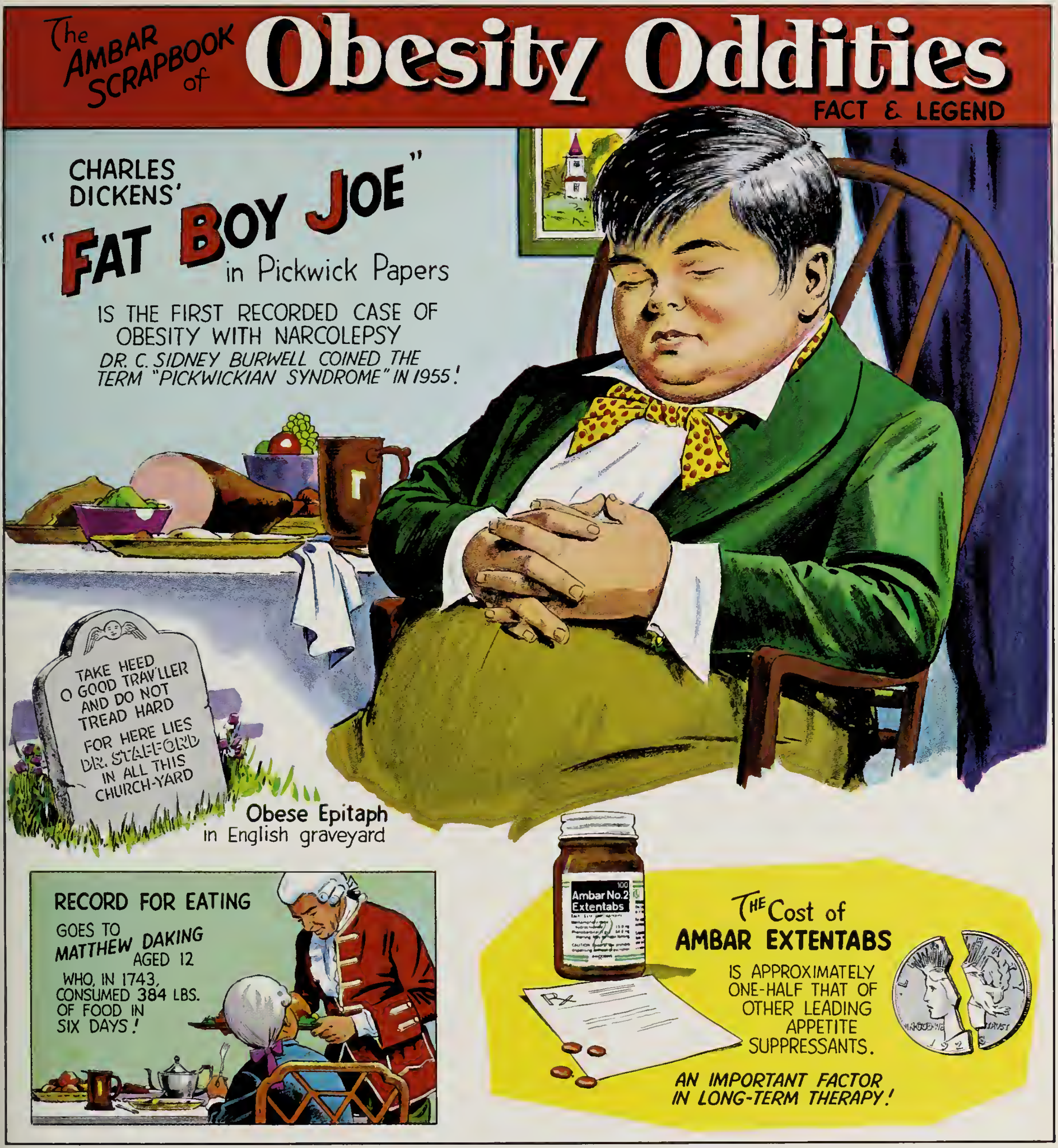
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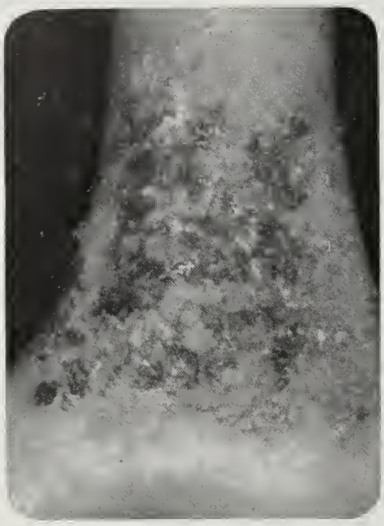
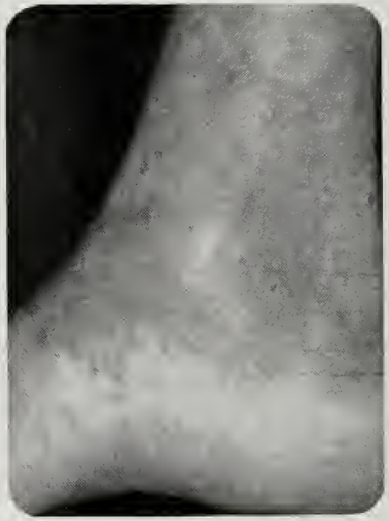


*Before treatment*



*After treatment*—
with ARISTOCORT Topical
Ointment 0.1% for two weeks

ARISTOCORT® Triamcinolone Acetonide Topicals have proved exceptionally effective in the control of various forms of eczema: allergic, atopic, nummular, psoriatic, and mycotic.

In most cases responsive to topical ARISTOCORT, the 0.1% concentration is sufficiently potent. The 0.5% concentration provides enhanced topical activity for patients requiring additional potency for proper relief.

*Administration and Dosage:* Apply sparingly to the affected area 3 or 4 times daily. Some cases of psoriasis may be more effectively treated if the 0.1% Cream or Ointment is applied under an occlusive dressing.

*Contraindications:* Tuberculosis of the skin, herpes simplex, chicken pox and vaccinia.

*Precautions and Side Effects:* Do not use in the eyes or in the ear (if drum is perforated). A few individuals react unfavorably under certain conditions. If side effects are encountered, the drug should be discontinued and appropriate measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive nonpermeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyodermas will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

Available in 5 Gm. and 15 Gm. tubes and ½ lb. jars.

PHOTOGRAPHS COURTESY OF M. M. NIERMAN, M.D.

**Aristocort®** Topical Ointment 0.1% and Cream 0.1%, 0.5%
Triamcinolone Acetonide

Also available in foam form.

Lederle LEDERLE LABORATORIES, A Division of American Cyanamid Company, Pearl River, New York

406-6

# BREAK A DIET CYCLE, TODAY.

On-again, off-again dieting is the worst kind.

On the 8th day of most "7-day diets," people are too busy eating to tell you how much they lost.

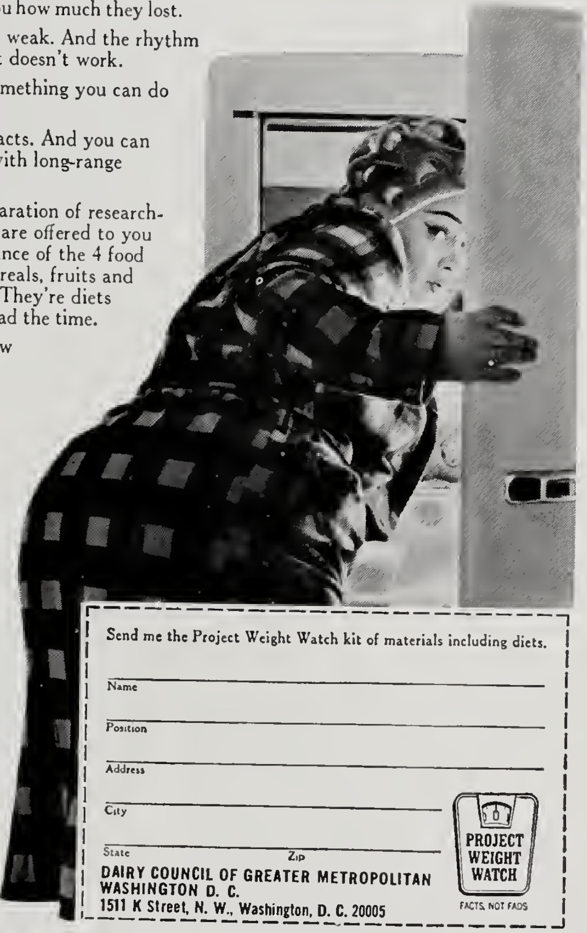
It's just that week diets are weak. And the rhythm method of girth control just doesn't work.

As a professional, there's something you can do about it.

You can replace fads with facts. And you can supplant short-term plans with long-range easy-to-follow diets.

That's what prompted preparation of research-tested scientific diets which are offered to you free. They're a realistic balance of the 4 food groups—meat, bread and cereals, fruits and vegetables and dairy foods. They're diets you'd write yourself if you had the time.

Send for them. Fasts are slow ways to lose weight.



Send me the Project Weight Watch kit of materials including diets.

Name

Position

Address

City

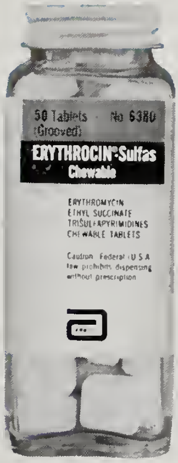
State Zip

**DAIRY COUNCIL OF GREATER METROPOLITAN WASHINGTON D. C.**
1511 K Street, N. W., Washington, D. C. 20005

PROJECT WEIGHT WATCH
FACTS, NOT FADS

Perhaps there have been times when you wanted to prescribe erythromycin and triple sulfas for little patients. Now you can—with a choice of two new fine-tasting pediatric forms.

# **New**–Two Pediatric Forms of Erythromycin and Triple Sulfas


50 Tablets No. 6380
(Grooved)
ERYTHROCIN®Sulfas
Chewable
ERYTHROMYCIN ETHYL SUCCINATE TRISULFAPYRIMIDINES CHEWABLE TABLETS
Caution: Federal (U.S.A.) law prohibits dispensing without prescription

No. 6372
For Oral Suspension
ERYTHROCIN®Sulfas
Granules
ERYTHROMYCIN ETHYL SUCCINATE TRISULFAPYRIMIDINES FOR ORAL SUSPENSION
ERYTHROCIN®Sulfas
Granules

## ERYTHROCIN®-SULFAS Chewable

(Erythromycin ethyl succinate-trisulfapyrimidines chewable tablet)

In clinical trials[1,2], this orange-flavored tablet was given to 55 patients, aged four months to 18 years.

Diagnoses (multiple in some cases) represented a cross section of bacterial infections commonly seen in pediatric office practice.

Therapy was given from three to 12 days, with an average of six days.

Of the 55 patients, 30 were reported cured within 72 hours, while 22 showed partial recovery within the same time, and subsequent clinical cure.

**A clinical cure rate of 94.5%**

## ERYTHROCIN®-SULFAS Granules

(Erythromycin ethyl succinate-trisulfapyrimidines granules for oral suspension)

87 patients were treated[1,2]—all children, ages four months to 15 years.

The diagnoses were multiple in some cases and were chiefly bacterial infections of the respiratory tract.

Dosage was maintained from three to 10 days; average treatment was five days. All of the ill children accepted the orange-flavored suspension favorably.

53 were clinically cured within 72 hours, while 32 showed partial relief within the same time, and subsequent clinical cure.

701358

**A clinical cure rate of 97.7%**

ABBOTT

Brief Summary on next page

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1. Case Reports on File, Dept. Clin. Development, Abbott Laboratories.
2. Polley, R.F.L., Use of Erythromycin-Sulfas in Office Practice, Western Med., 7:177, July, 1966.

ERYTHROCIN®-SULFAS
Brief Summary

**Contraindications:** Known sensitivity to erythromycin or sulfonamides. Because of the possibility of kernicterus with sulfonamides, do not use in pregnancy at term, premature or newborn infants.

**Warnings:** As with other forms of sulfonamide therapy, carefully evaluate patients with liver or kidney damage, urinary obstruction, or blood dyscrasia. Deaths have been reported from hypersensitivity reactions and blood dyscrasias following use of sulfonamides. Perform blood counts and liver and kidney function tests if used repeatedly at close intervals or for long periods.

**Precautions, Side Effects:** Occasionally mild abdominal discomfort, nausea or vomiting may occur with erythromycin, generally controlled by reduction of dosage. Mild allergic reactions (such as urticaria and other skin rashes) may occur. Serious allergic reactions have been extremely infrequent. Use sulfonamides with caution in patients with a history of allergy. Assure adequate fluid intake to prevent crystalluria and institute alkali therapy if indicated. If overgrowth of nonsusceptible organisms occurs, withdraw the drug and institute appropriate treatment. If a patient should show signs of hypersensitivity, appropriate countermeasures (e.g. epinephrine, steriods, etc.) should be administered and the drug withdrawn.

**Adverse Reactions:** Sulfonamide therapy may be associated with headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.

Side effects due to erythromycin are infrequent, but occasional abdominal discomfort, nausea, or vomiting, urticaria and other skin rashes may occur.

**Supplied:** The Granules for Oral Suspension come in bottles of 60 ml. and 150 ml. The Chewable tablets are in bottles of 50. Each 5-ml. teaspoonful of reconstituted Granules or each Chewable tablet provides erythromycin ethyl succinate equivalent to 125 mg. of erythromycin activity and 167 mg. of each of sulfadiazine, sulfamerazine and sulfamethazine.

701358 ABBOTT

## NATIONAL AND REGIONAL MEETINGS

**November 19–22: Association of Military Surgeons of the United States. Sheraton-Park Hotel, Washington. Address: Brig. General Frank E. Wilson, USAR (Ret.), Executive Director, 1500 Massachusetts Avenue, N.W., Washington, D. C. 20005.**

**November 20–22: Annual Scientific Assembly, The Medical Society of the District of Columbia. Statler-Hilton Hotel, Washington. Address: Mr. George W. Cooley, Executive Director, 2007 Eye Street, N.W., Washington, D. C. 20006.**

November 26–29: American Medical Association (Clinical Convention). Houston, Texas. Address: Dr. F. J. L. Blasingame, Executive Vice President, 535 North Dearborn Street, Chicago, Ill. 60610.

November 29–December 3: American Medical Women's Association. Atlanta, Ga. Address: Mrs. Gertrude F. Conroy, Executive Director, 1740 Broadway, New York, N. Y. 10019.

**December 2: American College of Physicians (Maryland/D. C. Regional). Baltimore, Md. Address: Dr. Martin L. Singewald, 11 East Chase Street, Baltimore, Md. 21202.**

December 2–7: American Academy of Dermatology. Palmer House, Chicago. Address: Dr. Stanley E. Huff, Secretary, 636 Church Street, Evanston, Ill. 60201.

December 4–6: Southern Surgical Association. The Homestead, Hot Springs, Va. Address: Dr. George H. Yeager, 314 Medical Arts Building, Baltimore, Md. 21201.

December 26–31: American Association for the Advancement of Science. New York. Address: Dr. R. L. Taylor, 1515 Massachusetts Avenue, N.W., Washington, D. C. 20005.

January 14–18, 1968: Society for Cryo-Ophthalmology. Miami Beach, Fla. Address: Dr. John G. Bellows, Executive Secretary, 30 North Michigan Avenue, Chicago, Ill. 60602.

January 17–18: American Rheumatism Association. Baltimore. Address: Miss Margaret M. Walsh, 1212 Avenue of the Americas, New York, N. Y. 10036.

January 20–25: American Academy of Orthopaedic Surgeons. Palmer House, Chicago. Address: Mr. John K. Hart, 29 East Madison, Chicago, Ill. 60602.

March 22–23: Second National Congress on the Socio-Economics of Health Care. Palmer House, Chicago. Address: Council on Medical Service, American Medical Association, 535 North Dearborn Street, Chicago, Ill. 60610.

# BOOKS RECEIVED

Acknowledgment is made of the following books which have recently been received.

**Infant Nutrition.** Samuel J. Fomon, M.D. Price, $10.50. Pp. 299. Philadelphia: Saunders, 1967.

**The Office Assistant in Medical Practice,** 3rd ed. Portia M. Frederick and Mary E. Kinn, C.P.S. Price, $7.50. Pp. 461, illustrated. Philadelphia: Saunders, 1967.

**The Health Consequences of Smoking. A Public Health Service Review: 1967.** PHS Publ. No. 1696. Price, 60 cents. Pp. 199. Washington, D.C. 20402: U.S. Government Printing Office, 1967.

**Gynecologic Pathology.** Frederick T. Kraus, M.D. Price, $18.50. Pp. 504, with 488 illustrations. St. Louis: Mosby, 1967.

**Manual of Preoperative and Postoperative Care** by the Committee on Pre and Postoperative Care, American College of Surgeons. Editorial Subcommittee: Henry T. Randall, M.D., Chairman; James D. Hardy, M.D., and Francis D. Moore, M.D. Price, $8.50. Pp. 506. Philadelphia: Saunders, 1967.

**Caste and Race: Comparative Approaches.** A Ciba Foundation Volume. Edited by Anthony deReuck and Julie Knight. Price, $12.00. Pp. 348. Boston: Little, 1967.

**Ciba Foundation Symposium: Development of the Lung.** Edited by A. V. S. deReuck, M.Sc., D.I.C., A.R.C.S., and Ruth Porter, M.R.C.P. Price, $13.00. Pp. 408, with 134 illustrations. Boston: Little, 1967.

**Insurance for the Doctor.** Harvey Sarner, LL.B., and Herbert C. Lassiter, LL.B. Price, $9.00. Pp. 193. Philadelphia: Saunders, 1967.

**Handbook of Orthopaedic Surgery,** 7th ed. Alfred R. Shands, Jr., B.A., M.D., F.A.C.S., R. Beverly Raney, Sr., B.A., M.D., F.A.C.S., with the collaboration of H. Robert Brashear, B.A., M.D., F.A.C.S. Price, $12.00. Pp. 572, with 269 illustrations. St. Louis: Mosby, 1967.

**Respiratory Physiology.** N. Balfour Slonim, M.D., Ph.D., and John L. Chapin, Ph.D. Price, $8.75. Pp 199, with 41 illustrations. St. Louis: Mosby, 1967.

**Ciba Foundation Study Group No. 28: Thiamine Deficiency: Biochemical Lesions and Their Clinical Significance.** Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Maeve O'Connor, B.A. Price, $4.50. Pp. 163, with 46 illustrations. Boston: Little, 1967.

**Ciba Foundation Colloquia on Endocrinology, Volume 16: Endocrinology of the Testis.** Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Maeve O'Connor, B.A. Price, $12.50. Pp. 331, with 93 illustrations. Boston· Little, 1967.

One by one
the family's downed
Because the
G.I. bug's around

Parepectolin for quick relief of acute diarrhea
...soothes colicky pain with paregoric*
...consolidates fluid stools with pectin
...adsorbs irritants with kaolin,
and protects intestinal mucosa.

Whether it's a 24-hour "bug", a food problem, or simply nervousness and anxiety, Parepectolin will bring the diarrhea under control until etiology can be determined. In some cases, Parepectolin may be all the therapy necessary.

Parepectolin®

Each fluid ounce of creamy white suspension contains:
*Paregoric (equivalent) ........ (1.0 dram) 3.7 ml.
Contains opium (¼ grain) 15 mg. per fluid ounce.
*warning: may be habit forming*
Pectin .................... (2½ grains) 162 mg.
Kaolin (specially purified) .... (85 grains) 5.5 Gm.
(alcohol 0.69%)
Usual Adult Dose: One or two tablespoonfuls three times daily.
Usual Children's Dose: One or two teaspoonfuls three times daily.

RORER
WILLIAM H. RORER, INC.
Fort Washington, Pa.

# Dear Doctor:

Wouldn't you like your patients to learn more about the contributions made by the world of medicine to their welfare? So that they can better appreciate the efforts of the health team to keep them in good health?

To tell the stories of medical and pharmaceutical advances to people throughout the country, the Pharmaceutical Manufacturers Association is sponsoring a unique "magazine within a magazine." It is called *Medicines and your family's health* and the first issue appears in the November *Reader's Digest*.

We would like to send you 50 free reprints of *Medicines and your family's health* for use in your reception room. Your patients will find the articles in this issue factual, educational and of immediate personal interest.

Just fill out the coupon below and send it to us.

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Gentlemen:
Please send me 50 free copies of
*Medicines and your family's health.*

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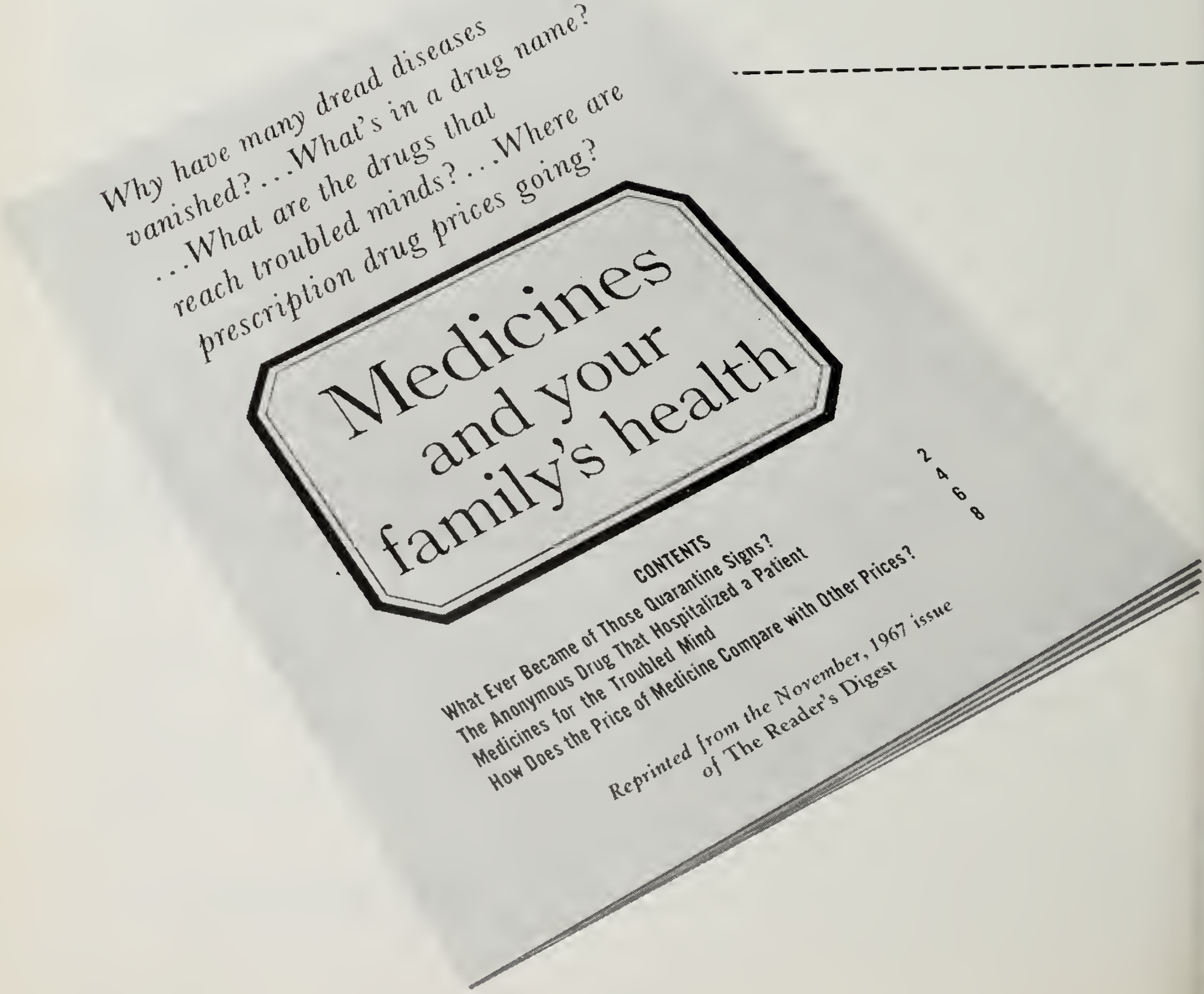


*Why have many dread diseases vanished? ...What's in a drug name? ...What are the drugs that reach troubled minds? ...Where are prescription drug prices going?*

Medicines and your family's health

2 4 6 8

CONTENTS

What Ever Became of Those Quarantine Signs?
The Anonymous Drug That Hospitalized a Patient
Medicines for the Troubled Mind
How Does the Price of Medicine Compare with Other Prices?

*Reprinted from the November, 1967 issue of The Reader's Digest*

# Dulcolax®

bisacodyl

DU-5255 R

Few drugs work as predictably as Dulcolax. You can expect that when your office patient takes Dulcolax at home, it will be as effective as you said it would be. Your patient will be gratified, too.

The reliability of Dulcolax stems from its unique mode of action. The drug works directly on nerve endings in the colonic mucosa, producing normal peristalsis throughout the large intestine. It does not rely on systemic absorption for its effect.

This reliable action provides prompt relief of constipation. It also makes Dulcolax particularly useful for prepping the bowel for special procedures. In short, it makes Dulcolax ideal for your office practice.

11 12 1
10 2
9 3
8 4
7 6 5
predictable bowel evacuation

Dulcolax acts so surely that the time of evacuation can often be closely predicted. Dulcolax tablets taken at night almost invariably result in a bowel movement soon after waking the following morning. Dulcolax suppositories generally work in 15 to 20 minutes, almost always within the hour.

General Dosage Information: *Adults:* When an ordinary laxative effect s desired, 1 to 3 tablets or 1 suppository usually suffices. Tablets nust be swallowed whole, not chewed or crushed, and should not be aken within one hour of antacids or milk. *Children:* 1 or 2 tablets, lepending on age and severity of condition. Tablets must not be given o a child too young to swallow them whole. For infants and children inder 2 years of age, half a suppository is usually effective. Above this ge a whole suppository is usually advisable. Side Effects: As with any axative, abdominal cramps are occasionally noted, particularly in severely constipated persons. High dosage may result in loose, unformed stools. Contraindication: Contraindicated only in acute surgical abdomen. Availability: Tablets (5 mg.) and suppositories (10 mg.). By prescription or recommendation.

Under license from Boehringer Ingelheim G.m.b.H.

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation, Ardsley, N.Y.

"Yes, Doctor, the pain is gone."

**'EMPIRIN'® COMPOUND with CODEINE PHOSPHATE gr. 1/2 No. 3**

Each tablet contains: Codeine Phosphate gr. ½ (Warning – May be habit forming), Phenacetin gr. 2½, Aspirin gr. 3½, Caffeine gr. ½.

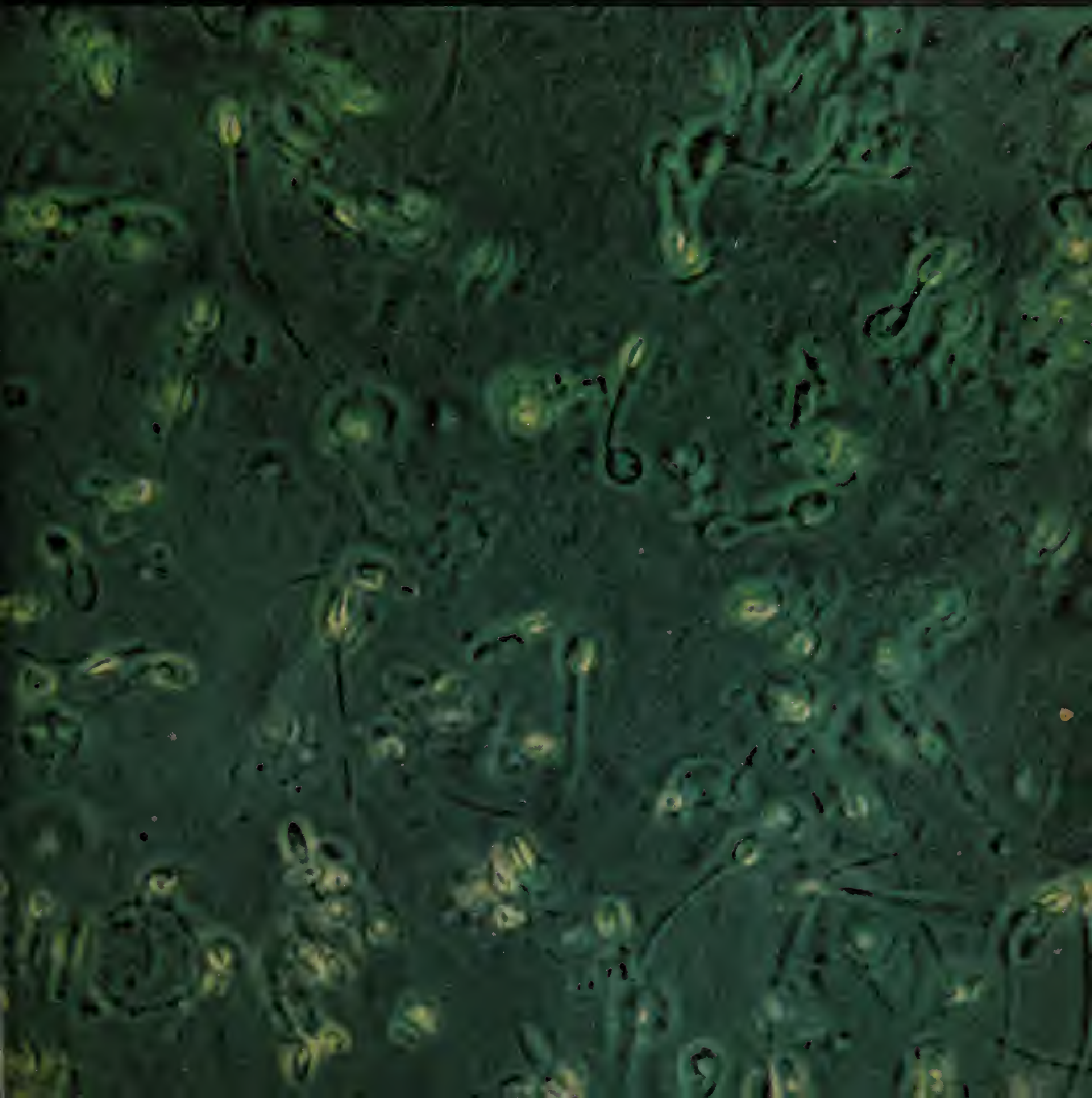
■ Despite introduction of synthetic substitutes, efficacy of 'Empirin' Compound with Codeine remains unchallenged.

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N.Y.

When the talk turns to oral contraceptives, it makes medical sense to remember low-dose Norinyl®-1.

(norethindrone 1mg. c̄ mestranol 0.05mg.)

Turn page for contraindications, precautions and side effects.



Reduction of oral contraceptive dosage to the lowest effective levels is a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now also available as Norinyl-1, containing exactly one half the previous dosage of norethindrone and mestranol. Clinical experience has established that effective fertility control can be achieved with the same degree of reliability and safety with new Norinyl-1 when taken as directed.

What about switching patients from higher dosage forms?

In transferring patients to low-dose Norinyl-1 from higher-dosage oral contraceptives, some breakthrough bleeding may occur in the early cycles. In the majority of cases the bleeding episode is mild and self-limited. The long-term advantages of the lower dosage form should be weighed against the inconvenience of possible breakthrough bleeding in the individual patient.

*Prescribing Information*

*Contraindications:* Patients with any symptoms or history of thrombophlebitis, pulmonary embolism, liver dysfunction or disease, carcinoma of breast or genital organs, or undiagnosed vaginal bleeding.

*Warnings:* Discontinue medication pending examination if there is sudden partial or complete loss of vision, proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. The safety of Norinyl-1 in pregnancy has not been demonstrated. If a patient misses two consecutive periods, pregnancy should be ruled out before continuing the medication. If she has not adhered to the prescribed schedule, pregnancy should be considered at the first missed period. Active ingredients of oral contraceptives have been detected in the milk of mothers who received these drugs; the significance to infants has not been determined.

*Precautions:* Pretreatment physical should include examination of the breasts and pelvic organs, as well as a Papanicolaou smear. If endocrine or liver function tests are abnormal during therapy, repeat tests are recommended after the drug has been withdrawn for two months. Following administration of drug, preexisting uterine fibromyomata may increase in size. Careful observation and caution are required for patients with symptoms or history of epilepsy, migraine, asthma, cardiac or renal dysfunction, cerebrovascular accident, psychic depression, and diabetes. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. Possible long-term effects of the drug on pituitary, ovarian, adrenal, hepatic or uterine function must await further studies. The physician should be alert to the earliest manifestations of thrombophlebitis and pulmonary embolism. The drug should be used judiciously in those young patients in whom bone growth is not complete. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask symptoms of the climacteric. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

*Side Effects:* The following have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals, mental depression. Although the following side effects have been reported in users of oral contraceptives, no cause and effect relationship has been established: anovulation posttreatment, premenstruallike syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, an itching. The following occurrences have been observed in users of oral contraceptives (a cause and effect relationship has neither been established nor disproved): thrombophlebitis, pulmonary embolism, neuroocular lesions.

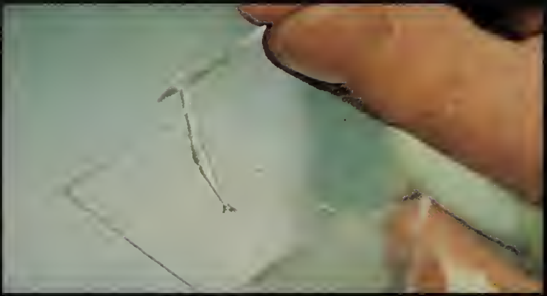
The following laboratory tests may be altered by the use of oral contraceptives: increased sulfobromophthalein and other hepatic functio tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in $T^3$ values), metyrapone test, pregnanediol determination.

norethindrone — an original steroid from
SYNTEX
LABORATORIES INC., PALO ALTO, CALIF.

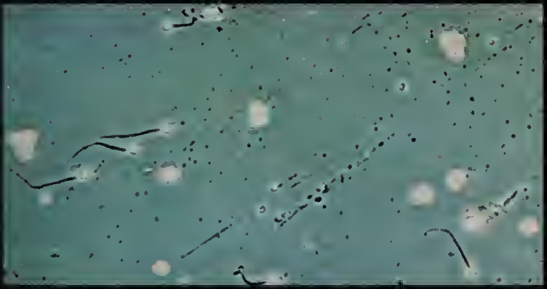
# Here's why Norinyl-1 makes medical sense.

The effectiveness of Norinyl-1 as a low-dose oral contraceptive may be explained by its possible multiple action. In addition to its primary action of suppression of ovulation, Norinyl-1 may offer additional protective mechanisms... (1) creation of a cervical mucus that may be hostile to sperm penetration, and (2) development of an endometrium that may be out of phase with nidation. These effects are illustrated below.

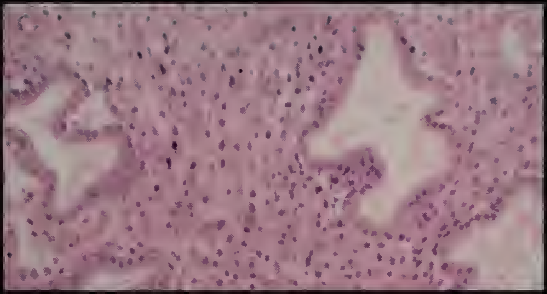
**Untreated Patient**



Cervical mucus at midcycle is usually thin and watery, with Spinnbarkeit (stretchability) of 15 to 20 cm.

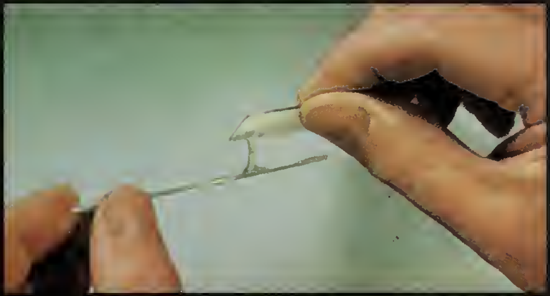


Spermatozoa appear healthy, active, freemoving.

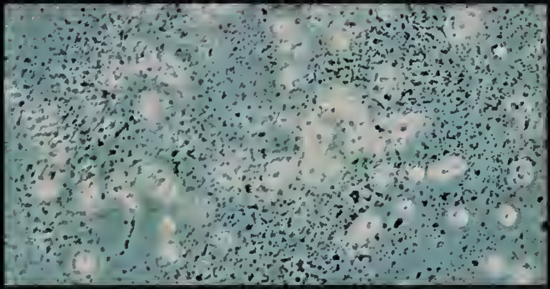


Endometrium of untreated patient is receptive to the fertilized ovum during secretory phase.

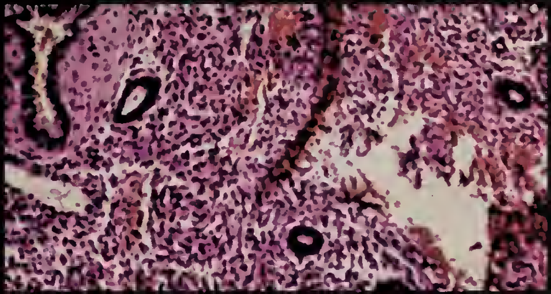
**Norinyl-1 Patient**



Cervical mucus at midcycle is scanty, viscous—with Spinnbarkeit of 1 cm. or less.



Immobile spermatozoa as they appear in cervical mucus taken from patient treated with Norinyl-l.



Norethindrone in Norinyl-l accelerates secretory phase, suppresses glandular and vascular development.

**Norinyl®-1** tablets
(norethindrone 1mg. c̄ mestranol 0.05mg.)

- new low dose of time-proved ingredients
- established norethindrone/mestranol ratio
- lower patient cost

# An uncommon steroid for common inflammatory dermatoses

In everyday topical steroid therapy, Synalar produces rapid resolution of inflammation and itching in steroid-responsive dermatoses—and at relatively low cost to the patient.

**Advanced molecular design enhances potency**

Synalar combines the advantage of earlier corticosteroid compounds with unique structural innovations. As a result, preparations of Synalar 0.01% and Synalar 0.025% have been reported to be more potent topically and significantly more effective than hydrocortisone 1.0%. The unique fluocinolone acetonide molecule provides one of the most useful topical corticosteroids for everyday practice.

**Impressive clinical results in a wide range of dermatologic problems**

The clinical efficacy of Synalar has been extensively documented in the world literature. Commonly encountered diseases such as allergic and contact dermatitis, eczematous and seborrheic dermatitis, and neurodermatitis respond rapidly to Synalar, often where previous therapy with other topical corticosteroids has failed.

**Low patient cost for wider usefulness**

With Synalar, a high degree of efficacy does not mean high price. And—a small quantity goes a long way. Thus, your patients can often obtain the "economy" of a hydrocortisone preparation with the proved efficacy of a potent, truly advanced steroid.

**Synalar®**
fluocinolone acetonide

Turn page for contraindications, precautions and side effects

# For everyday topical steroid therapy
# **Synalar® 0.01%**
# fluocinolone acetonide
# provides economy in two practical dosage forms

For general use, the most economical and widely applicable concentration of Synalar is 0.01% Cream in a water-washable, vanishing cream base. Synalar Solution 0.01% is especially valuable in dermatoses involving moist, intertriginous areas or hairy sites where creams and ointments do not spread or penetrate readily. Synalar Solution is a unique dosage form—clear, nongreasy, cosmetically elegant.

*Product Information*

*Contraindications:* Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. *Precautions:* Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. *Side Effects:* Side effects are uncommon with topical corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. In such cases the agent should be discontinued and appropriate measures taken. *Availability:* Synalar (fluocinolone acetonide) Cream 0.025%—5, 15 and 60 Gm. tubes and 425 Gm. jars. Cream 0.01%—15, 45 and 60 Gm. tubes and 120 Gm. jars. Solution 0.01%—20 and 60 cc. plastic squeeze bottles. Ointment 0.025%—15 and 60 Gm. tubes. Neo-Synalar® (neomycin sulfate 0.5% [0.35% neomycin base], fluocinolone acetonide 0.025%) Cream—5, 15 and 60 Gm. tubes.

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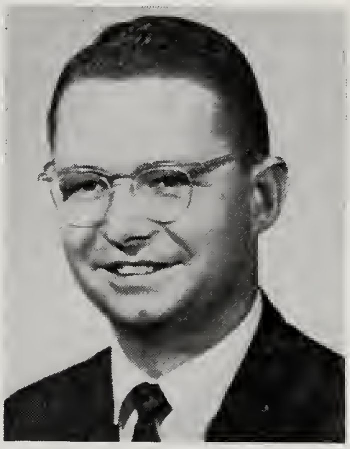

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MEDICAL ANNALS

*of the District of Columbia*

*November 1967* VOLUME XXXVI • NUMBER 11

## Howard University Number

THIS IS THE THIRD of a fifth series of special numbers of the MEDICAL ANNALS, the scientific material for which is supplied by medical institutions and scientific organizations in the Washington Metropolitan Area. For the HOWARD UNIVERSITY NUMBER the Editorial Board is indebted to Dr. W. Montague Cobb, Consulting Editor of the MEDICAL ANNALS, who secured the papers which appear in this issue.

# Studies in Sickle-cell Anemia

## XXXII. Roentgenographic Aspects of Osseous Changes*

CAPTAIN ALBERT JOHNSON, JR., USAF, MC,† T. WILKINS DAVIS, M.D.,‡
ANGELLA D. FERGUSON ,M.D.,§ AND ROLAND B. SCOTT, M.D.‖

IN A PREVIOUS STUDY[1] we described the gross and microscopic pathological changes in the osseous system as observed in autopsy material from patients with sickle-cell anemia. This report is concerned primarily with radiographic observations on skeletal tissues in living patients with this disease. We have compared our findings with those of other investigators as recorded in the medical literature.¶

### Materials and Methods

The bones of 83 Negro patients diagnosed as having sickle-cell anemia (SCA) were studied radiographically in our hospital. The subjects were grouped into the following specific age categories: infancy, early childhood, middle childhood, late childhood, adolescence, and adult.

The X-ray findings in the skeletal system of 394 patients with SCA as reported by various investigators in the literature were reviewed. Of this number it was possible to classify 171 patients into the aforementioned age categories. The remaining 223 cases were not used in this comparative study because age was not specified. However, the changes described were consistent with the general roentgenographic findings described for SCA patients in our series.

### Results

The comparative incidence of osseous changes noted in the 2 groups of patients is presented in figure 1.

In evaluating the results presented here it should be noted that the majority of cases obtained from the literature survey are from the older or adult age group and the sample obtained from the Freedmen's Hospital study (our series) involves mainly the pediatric age group. Table 1 summarizes the actual number of cases in each age category from the 2 sources.

*Skull.* Studies of the X-ray films of the skull gave strong evidence that the most significant changes in the cranial bones occur in the earlier years (infancy through childhood). In both series

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* This project was supported in part by research grants from the Sickle Cell Disease Research Foundation of Los Angeles, California.

† Present address: Brooks Air Force Base, San Antonio, Tex. 78235. This study was pursued during the summers of 1963, 1964 and 1965 when the senior author served as a student research fellow in the Department of Pediatrics at the Howard University College of Medicine.

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¶ A bibliographic listing of 30 articles dealing with bone involvement in sickle-cell anemia is available upon request to the authors. (Address requests to Dr. Scott.)

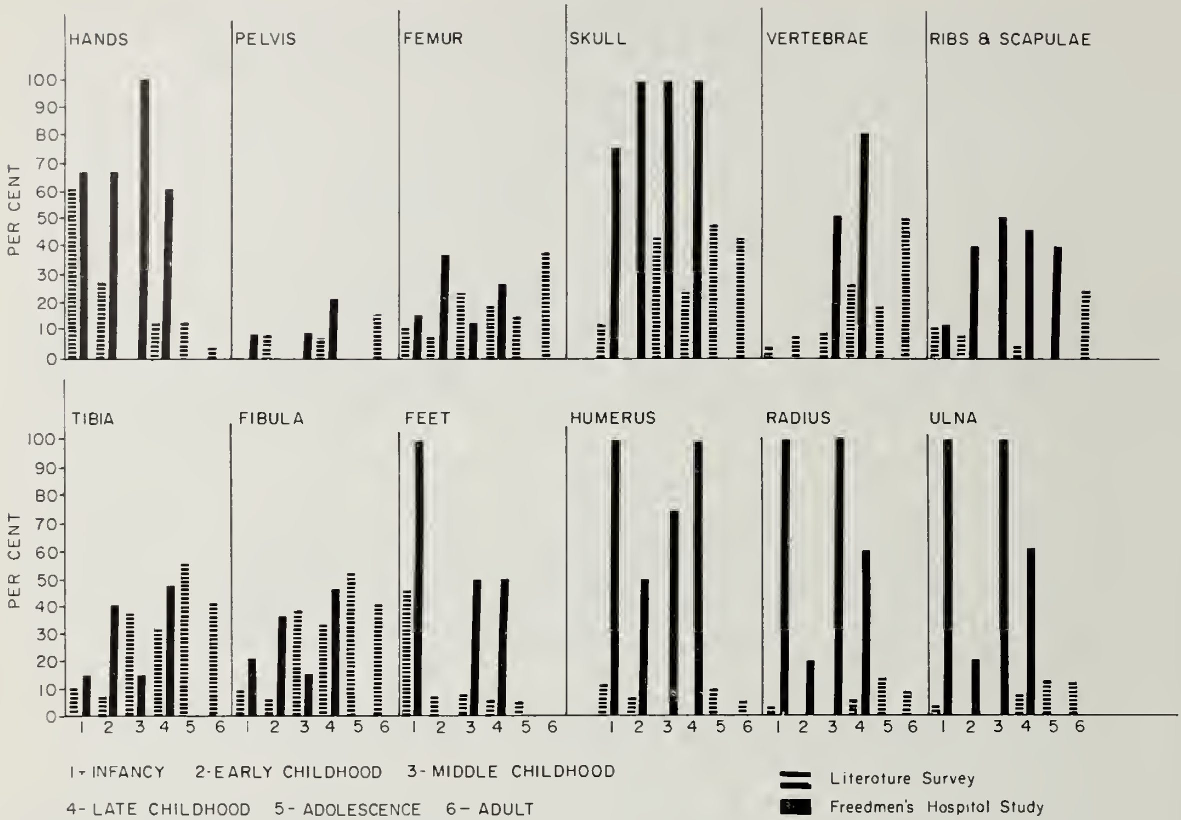

**FIG. 1. Graphic representation of osseous changes in 83 patients from our hospital compared with similar findings of other authors. The generally higher incidence of bony abnormalities in our material is attributed to the younger age of our patients. Certain changes occurring in children are reversible and disappear with advancing age.**

**TABLE 1: Number of Cases in Each Age Category in the Literature Series and the Freedmen's Hospital Series**

| Age Categories | Literature | | Freedmen's Hospital | |
|---|---|---|---|---|
| | No. Cases | Per cent | No. Cases | Per cent |
| Infancy (birth–2 years) | 31 | 18 | 14 | 17 |
| Early childhood (3–6 years) | 15 | 9 | 22 | 27 |
| Middle childhood (7–10 years) | 16 | 9 | 26 | 31 |
| Late childhood (11–16 years) | 33 | 20 | 15 | 18 |
| Adolescence (17–21 years) | 29 | 17 | 1 | 1 |
| Adult (22–60 years) | 47 | 27 | 5 | 6 |

of studies the skull was the most frequently involved osseous tissue, irrespective of age. There was noted a thinning of the outer table and widening of the diploic spaces. In our study there were 3 children with the "hair-on-end" X-ray appearance (figure 2). In each case the patient was less than 5 years old (11 months, 1 year, and 3 years). This finding alone is not diagnostic of blood dyscrasias since it has been observed in children with other disorders.

*Hands and feet.* It has been pointed out that swelling of the hands and feet occurs frequently enough in the infant with SCA to warrant an immediate suspicion of this disease (hand-foot syndrome). Our study confirms this finding and reveals that this syndrome is also observed occasionally in late childhood. These osteolytic changes

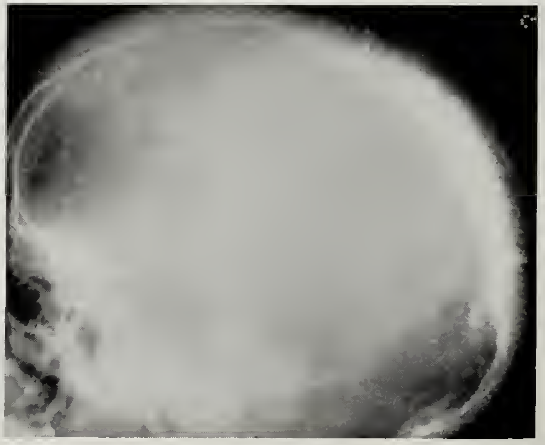

**FIG. 2. Widening of diploic space and thinning of outer table with radial striations of diploic trabeculae to give "hair-on-end" appearance.**

take the form of areas of destruction and repair of varying degrees, often with periosteal reaction (figure 3). The highest incidence of modification in the bones of the hands and feet occurred in infancy and childhood in both series.

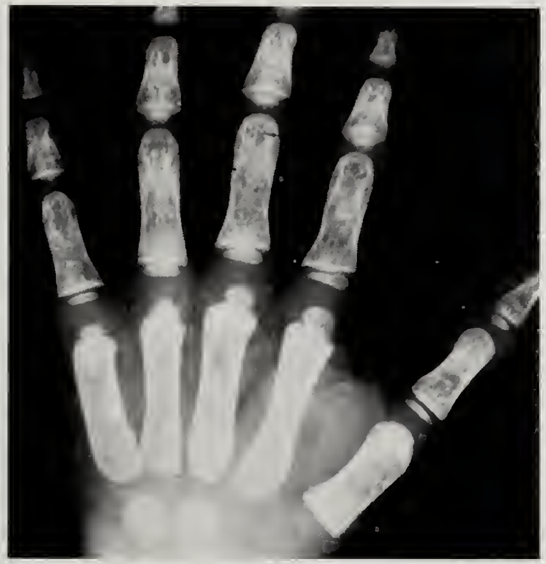

**FIG. 3. Generalized osteolytic changes characterized by areas of destruction and accentuation of trabecular markings and variable periosteal reaction.**

*Radius, ulna and humerus.* Other investigators reported that changes in the radius and ulna occur infrequently during infancy and childhood but are often found during adolescence and in the adult. In contradistinction, 94.0 per cent of all children from the Freedmen's Hospital study showed significant changes in these bones during infancy and childhood years. In both studies the highest incidence of osseous manifestations in the humerus was noted in infancy.

*Femur, tibia and fibula.* Changes are frequent in these structures. However, the incidence reported in the literature is less than that observed in our study. A probable explanation is that during childhood and adolescence vigorous utilization of the lower extremities occurs in play and in sports. The femoral and humeral heads are common sites for infarction in older children and adults leading to aseptic necrosis (figure 4). We observed a higher incidence of change in these osseous structures than was reported in the literature. Roentgen alterations in the femur were variable; the highest incidence was observed in early childhood in our series and in the adult in the literature study. The changes in the tibia and fibula in both series were similar and reached a peak incidence in adolescence. The lowest incidence of alteration occurred in infancy.

*Vertebrae.* According to other investigators, striking changes occur in the vertebrae during infancy and advance through the various stages of life. Our findings are similar. Osteoporosis of the spine is probably one of the most consistent skeletal changes in sickle-cell disease. Once it is noted on X-ray films it is persistently found throughout all age periods.

*Ribs, scapulae and pelvis.* Changes in the ribs and scapulae followed a progressive pattern with age to reach a peak in middle childhood. From this point there was a trend toward a gradual decline in osseous manifestations varying inversely with the age of the patient. X-ray films of the thorax may demonstrate osteoporosis and areas of patchy sclerosis in the ribs and scapulae. These are valuable findings because when associated with an enlarged heart and pulmonary vascular congestion, one should consider a diagnosis of SCA, particularly in Negro patients.

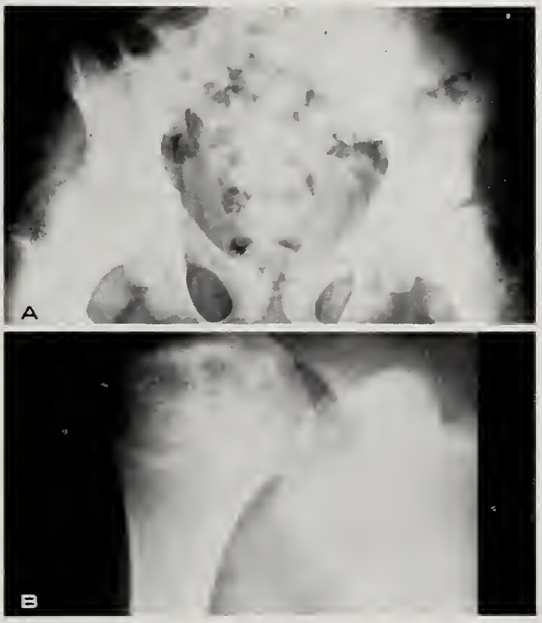

**FIG. 4. A. Aseptic necrosis secondary to infarction involving femoral heads and leading to flattening and fragmentation. B. A similar lesion is shown involving the head of the humerus which exhibits areas of increased and decreased density.**

## Discussion

Apparently less than 50 per cent of patients with SCA have significant bone changes on X-ray examination and only a few of these will exhibit involvement which can be regarded as characteristic for this disease. Many of the roentgen findings observed in SCA are similar to those seen in other blood dyscrasias, such as thalassemia and leukemia. These must be differentiated by their particular clinical and laboratory findings.

A number of other conditions produce bone changes which must be differentiated radiographically from SCA. If isolated areas within the bone show defects, there may be confusion with caisson disease which also produces multiple bone infarcts. An adequate history would enable one to rule out this condition. Hemangiomas of the vertebral body may simulate the coarse trabecular pattern seen in anemias; however, hemangiomas are usually singular and typically involve only 1 vertebral body. The flattening of the femoral heads due to aseptic necrosis seen in SCA simulates osseous manifestations produced by tuberculosis, osteomyelitis and Legg-Calvé-Perthes' disease. The dactylitis of congenital syphilis could cause diagnostic confusion, but syphylitic dactylitis is usually limited to 1 or 2 segments, whereas the anemias cause a more generalized involvement.

The roentgen findings in SCA are more valuable in arousing a suspicion of the presence of this blood dyscrasia than in making a definitive diagnosis. Hematologic and other diagnostic studies should always be employed.

### Summary

The roentgenographic changes in the bones of 83 patients with homozygous sickle-cell anemia were reviewed and compared with osseous findings in 171 patients reported in the medical literature by various investigators. Significant osseous changes have been noted to occur in all the bones of patients with sickle-cell anemia. The highest incidence of change was noted in the weight-bearing bones (tibia, femur, and vertebrae). Variations in bony architecture were variable in degree and, at least partially, reversible in most bones except the vertebrae, where alterations tended to be progressive. The roentgen findings in SCA are more valuable in arousing a suspicion of this disease than in making a definitive diagnosis.

### Reference

1. Johnson, A., Ferguson, A. D., Jackson, M. A., and Scott, R. B.: Studies in sickle-cell anemia. XXIX. Pathological aspects of osseous changes. J. Nat. Med. Ass., 1966, 58, 239.

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## Washington (D.C.) Area Professions Disaster Training Seminar

"Community Emergency Health Preparedness—The Team Approach" was the theme of the 1967 Professions Disaster Training Seminar which was held at the Washington Hospital Center on September 14 and 15.

The Seminar was sponsored by the Health Mobilization Division of the D. C. Department of Public Health, the Washington Area Medical and Dental Societies, the Hospital Council of the National Capital Area, the Health Facilities Planning Council for Metropolitan Washington, and nursing, pharmaceutical, dietetic, and veterinary organizations. Dr. John W. Latimer, Jr., Chairman of the Committee on Emergency Medical Services of the Medical Society of the District of Columbia, was moderator for the opening session.

In conjunction with the Seminar, on September 16 a disaster drill (Operation Fantom II) was initiated at the D. C. Armory, where "casualties" were treated, sorted, and sent to the participating hospitals. Umpire teams were also at the hospitals, which had activated their disaster programs to handle the casualties. The Disaster Physician in Charge of Operation Fantom II was Dr. W. Ronald Strong, Vice Chairman, Committee on Emergency Medical Services.

Chairman of Fantom II Communications Center, located at the Medical Society Headquarters, was Dr. Edwin Mitchell, a member of the Committee on Emergency Medical Services. Volunteers serving at the Medical Society Communications Center included members of local private radio operators' groups and the Woman's Auxiliaries to the Medical Society of D. C. and the Dental Society of D. C.

Participating in the training activities were physicians, dentists, veterinarians, pharmacists, nurses, dietitians, and other allied health personnel. Representatives were also present from the American Red cross, Civil Defense, Public Welfare, FBI, military organizations, fire and police departments, community volunteer groups, and press, TV, and radio.

# Medical Genetics: A Partner in Health Care

MIHALY BARTALOS, M.D.*

Medical genetics is a peculiar medical specialty with its own methods, own approaches, and its own jargon, comprehensible only to the initiated. Yet medical genetics in recent years has gained importance because of the many ways newer genetic knowledge can contribute to better patient care. In this short article, by limiting discussion to the diagnostic tools and therapeutic approaches presently practiced, an attempt is made to familiarize physicians with the ways genetic studies can contribute to the health of their patients.

### Medical Geneticist as a Clinician

In the many conditions which have some aspects placing them within the field of medical genetics, the medical geneticist must assume different roles. In some cases the task at hand is to determine the involvement of genetic factors in certain conditions. In others the involvement is known but the mode of inheritance needs clarification. Some condition with very similar clinical manifestations may be produced by different genetic mechanisms and/or also by environmental agents. The identification of the individual entities within such a heterogenous group of diseases is clearly desirable. Study of the nature of the genetic defect and establishing the mechanism how such defects lead to clinical manifestations are clearly a major aim of human genetic research. Once such a mechanism is understood at the molecular level, the requirements for finding effective therapeutic measures are provided.

Since no part of the body can escape the effect of genetic changes, medical genetics permeates all aspects of medicine. Medical genetics has several facets, one of them being clinical while the rest are aimed at increasing the effectiveness of clinical genetics. Like other clinical specialties, the aims of medical genetics include the establishment of correct diagnosis, effective therapy, a prognosis, an etiology, and preventive measures.

Since cases considered for studies by a medical geneticist can belong to any one of the established medical specialties, the specific procedures used and the specific training possessed by the medical geneticist can be of benefit to the patients of every physician. Thus it is in the interest of physicians, general practitioners, and specialists to get acquainted with the tools and methods used in medical genetics.

### Diagnostic Tools of Medical Genetics

Sex chromatin studies have been proven to be valuable adjuncts in the diagnosis of certain disorders affecting sexual differentiation. Sexual dimorphism of human cells was first demonstrated by Moore, Graham and Barr[1] in 1953 in the form of the presence of a small chromatin body in female nuclei adjacent to the inner aspect of the nuclear membrane. This finding is characteristic for normal female cells in the intermitotic or resting stage. Intermitotic somatic cells of normal males lack this cellular characteristic. It was later demonstrated that the "sex chromatin (Barr) body" is made up from a portion of one of the chromosomes involved in sex determination, the X chromosome. Normal females have 2 X chromosomes in their somatic cells of which one participates in sex-chromatin formation.

It is a well established fact that the number of sex chromatins is always 1 less than the number of X chromosomes in cells with a normal number of nonsex chromosomes. Thus normal males with 1 X and 1 Y sex chromosome have no sex-chromatin body in their cells, while patients with the Klinefelter syndrome and an XXY sex chromosome constitution as in normal females have 1 sex chromatin, and females with 3 X chromosomes have 2, and so on. If one records the percentage distribution of the sex-chromatin bodies encountered in different tissues and records their size, additional information can be obtained as to the probable chromosome constitution of the cells examined.

The study of the chromosomes is probably the best known diagnostic procedure in medical genetics despite the fact that its clinical usefulness was first demonstrated as recently as 1959. Since that time a number of clinical disorders have been demonstrated to be caused by abnormalities of the chromosomes. These include intersexuality, cases of infertility, a relatively high percentage of spontaneous abortions, multiple congenital malformations, some cases of mental retardation, and some forms of tumors (Bartalos and Baramki[2]).

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Specialized biochemical and biophysical studies have been found to be revealing in elucidating the nature of certain genetic conditions and have furnished useful diagnostic signs. The different kinds of electrophoresis are probably the best-known tools, used frequently for the determination of abnormal hemoglobins. Direct enzyme assays are necessary in many conditions in which variations in enzyme activity are suspected. The different chromatographic procedures, sometimes in combination with electrophoresis, are helpful in identifying the presence of abnormal metabolites. Among the biochemical screening procedures one can cite the widely known ferric chloride test, the urinary nitroprusside reaction, the qualitative Benedict's test, the dinitrophenylhydrazine test, and tests used for screening urinary metachromatic material.

Besides the cytological and the biochemical diagnostic tools there are others which do not need expensive laboratory equipment and highly trained laboratory personnel. One of these is the study of dermal ridge configurations on the palms and on the soles as well as on the fingers. These dermatoglyphic studies can provide supporting evidence in doubtful diagnosis (Bartalos[3]). The presence of characteristic dermatoglyphic findings in several genetic disorders is believed to result from the fact that dermal ridge configurations are determined by a large number of genes, the alteration of some of which can result in characteristic changes in dermal ridge patterns.

Many hereditary diseases are syndromes, meaning that characteristic alterations are observed in many organs occurring together. This feature of genetic syndromes is quite helpful, since those manifestations which are external and easily detected can provide useful clues for the diagnosis of serious internal disease.

Family history can likewise provide useful diagnostic clues in several hereditary diseases. Since there are different modes of inheritance, one of which is characteristic of any of the hereditary diseases, the occurrence of the condition in other family members can help to reveal the mode of inheritance of the condition in question. In this way diseases with similar clinical manifestation but with different inheritance patterns can be distinguished. Family studies may contribute to correct diagnosis and thus facilitate appropriate management.

### Therapeutic Procedures in Hereditary Diseases

It is common belief that as far as therapeutic intervention is concerned there is not much to be done in genetic disorders. While it is true that therapy is the "short suit" of medical genetics, there are many diverse procedures available to help affected individuals. Such procedures include surgical intervention, drug administration, special dietary measures, and individualized teaching and psychologic guidance. The removal of an enlarged clitoris is a corrective surgical measure. Removal of an eye because of retinoblastoma represents a therapeutic measure. Replacement of affected organs, such as in the case of hereditary cystic disease of the kidneys, is a further example of surgical intervention. In still other instances surgical removal of certain organs which may be involved in the clinical manifestation of the disease can be beneficial. An example of this is the removal of the spleen in spherocytic hemolytic anemia.

Administration of drugs can accomplish many aims depending on their mechanism of action. If the problem is the accumulation of excessive metabolites due to a genetic defect, the use of drugs which can bind to the metabolite and be excreted from the body may be beneficial. The use of penicillamine in Wilson's disease is based on this principle. Some compounds can be used to inhibit adaptive enzymes causing the accumulation of unphysiologic metabolites responsible for clinical manifestations. This is believed to be accomplished in oxalosis by the administration of sodium hydroxymethane sulfonate. In some conditions therapeutic benefit can be achieved by artificial induction of certain enzymes. Barbiturates in hyperbilirubinemia or steroids in glycogen storage disease seem to accomplish this. Coenzyme supplementation is a further example of the biochemical approach to treatment of genetic diseases. An example of this is vitamin $B_6$ supplementation in cystathioninuria and in pyridoxine dependency. If the missing gene product is identified and available in large quantities, the replacement of such a gene product can be attempted. In genetically determined deficiencies of certain blood clotting agents or in diabetes mellitus the usual treatment is the replacement of the missing protein. Special dietary measures can be used in some conditions to reduce nonessential precursors of a metabolite which is accumulating in the body because of an enzyme defect. Elimination of lactose from the diet in galactosemia or reduction of phenylalanine intake in phenylketonuria are

(*Continued on page 722*)

# Massive Gastrointestinal Hemorrhage

## A Clinical Study

LASALLE D. LEFFALL, JR., M.D., F.A.C.S.,[*] JACK E. WHITE, M.D., F.A.C.S.,[†]
AND BURKE SYPHAX, M.D., F.A.C.S.[‡]

MASSIVE BLEEDING from the gastrointestinal tract remains a challenging and life-threatening problem. Much has been written concerning aids as well as pitfalls in the diagnosis and treatment of this entity. To determine factors affecting morbidity and mortality in these patients, we made an analysis of all such cases seen at the Freedmen's Hospital (teaching hospital for Howard University College of Medicine) for a 5-year period (1962–1966). The criteria for massive bleeding were modified after the classification of Darin[1] and included (1) 8 Gm. per cent or less hemoglobin concentration or 22 per cent or less hematocrit, (2) clinical shock, (3) 40 mm. Hg systolic blood pressure below the normal for the patient, and (4) unstable hemoglobin or hematocrit after 3 blood transfusions.

### Clinical Material

A total of 22 patients, 17 males and 5 females, were evaluated over the 5-year period. Their ages ranged from 25 to 87 years. The causes, sex distribution, and survival are shown in table 1. The most common cause of massive bleeding was duodenal ulcer, while sigmoid diverticulosis and typhoid fever were the only causes of massive hemorrhage from the lower gastrointestinal tract.

Data on the 8 patients subjected to emergency surgical intervention are given in table 2. The 3 patients with gastric ulcers were over 60 years of age and required emergency surgery. Subtotal gastrectomy with gastrojejunostomy was performed in all 3 patients, with 2 deaths. Only 2 of the 8 patients with bleeding duodenal ulcers required emergency surgery. One was treated by 75 per cent subtotal gastrectomy with gastrojejunostomy and the other by vagotomy, pyloroplasty and suture ligation of the bleeding ulcer. Both patients recovered.

A 53-year-old woman developed a stress ulcer near the gastric cardia 6 days after a Whipple pancreatoduodenectomy (including 75 per cent resection of stomach) for carcinoma of the head of the pancreas. Emergency suture ligation of the bleeding ulcer allowed her recovery. A 40-year-old woman with massive hemorrhage secondary to typhoid fever died after emergency right hemicolectomy. She received 39 units of blood during her hospital stay. A 62-year-old man underwent emergency surgery for presumed bleeding duodenal ulcer. At laparotomy no bleeding site was found even though gastrotomy (limited) was performed. Blind subtotal gastrectomy was then effected. Postoperatively the patient continued to bleed and died from continued blood loss. Autopsy revealed esophagogastric lacerations (Mallory-Weiss syndrome) as the source of the blood loss.

**TABLE 1: Etiology, Sex Incidence, and Survival of 22 Patients with Massive Gastrointestinal Hemorrhage**

| | Male | Female | Recovered | Died |
|---|---|---|---|---|
| Causes of Bleeding: | | | | |
| Duodenal ulcer | 7 | 1 | 8 | 0 |
| Gastric ulcer | 2 | 1 | 1 | 2 |
| Esophageal varices | 2 | 0 | 0 | 2 |
| Gastritis | 2 | 0 | 2 | 0 |
| Sigmoid diverticulosis | 2 | 1 | 3 | 0 |
| Stress ulcer (postoperative) | 0 | 1 | 1 | 0 |
| Typhoid fever | 0 | 1 | 0 | 1 |
| Mallory-Weiss syndrome | 1 | 0 | 0 | 1 |
| Unknown | 1 | 0 | 0 | 1 |
| TOTAL | 17 | 5 | 15 | 7 |

Of the 14 patients not having emergency surgery, 11 survived. Both patients with esophageal varices and the one with an unknown cause died. Hematologic studies performed in the latter patient shortly before his death suggested a clotting defect as his basic abnormality.

A history of recent aspirin ingestion was obtained in 6 patients—1 with gastritis, 1 with gastric ulcer, and 4 with duodenal ulcer. There was no history of the use of other drugs such as Indocin®, Butazoladin®, or cortisone.

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[†] Professor of Surgery, Howard University College of Medicine.

[‡] Professor and Head, Department of Surgery, Howard University College of Medicine.

## Discussion

When the patient with massive gastrointestinal hemorrhage is admitted he is given a sedative if he is restless. Blood is drawn for hemoglobin, hematocrit, type and cross match, and detection of clotting deficiencies. It is emphasized that studies to ascertain the presence of coagulation defects should be obtained prior to transfusion in patients with massive gastrointestinal bleeding. In upper gastrointestinal bleeding a bromsulfalein test is performed. The bromsulfalein excretion is usually abnormal in patients with liver damage sufficient to be associated with esophageal varices. However, in patients with varices from extrahepatic portal obstruction when the liver is undamaged, bromsulfalein excretion is often normal. Shock, fever, and old age increase the percentage of dye retained after 45 minutes. In our 2 patients with varices the bromsulfalein retention was over 20 per cent.

Vital signs are recorded and charted. Intravenous fluids are started with a plasma expander (dextran), saline, or Ringer's lactate solution, and then blood is given. A good history and physical examination are important, with a search for spider nevi, splenohepatomegaly, liver palms, palpable abdominal masses, jaundice, cachexia, and ascites. Hyperperistalsis is often found when blood is present in the small intestine. Hematemesis suggests that the lesion is in the esophagus, stomach, or proximal duodenum. If this is absent a Levin tube introduced into the stomach will frequently prove the presence of upper gastrointestinal hemorrhage, reveal evidence of continuing or recurrent bleeding, and provide an estimate of the amount lost.[2]

Using the Hampton technique one may demonstrate duodenal or gastric lesions by upper gastrointestinal X-ray examination. However, about 25 per cent of patients are too ill for barium studies in the first 24 hours. Further, active bleeding and residual clots make evaluation difficult. It must be remembered that a demonstrated lesion may not be the bleeding site.[3] Among our 7 patients with upper gastrointestinal bleeding requiring emergency surgery the bleeding site was demonstrated in 4 of the 5 patients who had a Hampton study performed. Three gastric ulcers and 1 duodenal ulcer were demonstrated. No lesion was seen in another patient with a duodenal ulcer, but at surgery a clot was found filling the ulcer crater. One patient with esophagogastric tears and another with the stress ulcer were considered too ill for barium studies. Emergency upper gastrointestinal X-ray examination is desirable if the patient's condition permits. However, in exsanguinating hemorrhage one must often rely upon a good history and physical examination for diagnosis.

The Einhorn string test as modified by Rappaport[4] and Traphagen and Karlen[5] has resulted in a simple, inexpensive, and relatively easy test. A radiopaque umbilical tape is swallowed, and after a suitable period an X-ray film of the abdomen is made. Fluorescein dye is then injected intravenously, and 4 minutes later the tape is rapidly withdrawn and examined under a Wood's light. By correlating fluorescence with the previous X-ray film good results have been reported. Although it is a simple test, technical problems in its performance and problems of interpretation have arisen. We believe that this

**TABLE 2: Data on the Eight Patients Having Emergency Surgery**

| Cause of Bleeding | Age | Sex | Operation | Result | Cause of Death |
|---|---|---|---|---|---|
| Gastric ulcer | 73 | M | Subtotal gastrectomy | D* | Pneumonia; congestive heart failure |
| Gastric ulcer | 84 | M | Subtotal gastrectomy | D | Pneumonia |
| Gastric ulcer | 67 | F | Subtotal gastrectomy | R† | |
| Duodenal ulcer | 44 | M | Vagotomy; pyloroplasty; suture ligation of ulcer | R | |
| Duodenal ulcer | 29 | M | Subtotal gastrectomy | R | |
| Stress ulcer (postoperative) | 53 | F | Suture ligation | R | |
| Typhoid fever | 40 | F | Right hemicolectomy | D | Continued hemorrhage |
| Mallory-Weiss syndrome | 62 | M | Subtotal gastrectomy (blind) | D | Continued hemorrhage |

* Died.
† Recovered.

test may be occasionally informative and is being used now on our service. It was not used on patients included in this study.

In a report of a series of 323 cases Hedberg[6] stated that when both endoscopy and X-ray examination were employed in rapid sequence accurate diagnosis was possible in 92 per cent of patients with massive upper gastrointestinal hemorrhage. When diagnostic maneuvers were delayed or when radiography preceded endoscopy, accuracy fell to 80 per cent, while the mortality ratio for nonvariceal hemorrhage rose from 5.5 to 19 per cent. We seldom used endoscopy, relying upon clinical, laboratory, and radiographic findings. These modalities afforded a diagnostic accuracy of 82 per cent. It is highly probable that esophagoscopy would have demonstrated the bleeding esophagogastric lacerations in our patient with the Mallory-Weiss syndrome.

Selective visceral arteriography has proved to be a reliable diagnostic adjunct in evaluating selected cases of gastrointestinal hemorrhage or blunt abdominal trauma. Its use is advocated in gastrointestinal hemorrhage which cannot be localized by conventional diagnostic methods. Experimental work suggests that active bleeding at the rate of at least 0.6 ml. per minute may be identified by the appearance of intraluminal contrast medium during late phases of the arteriogram. In the absence of active bleeding other arteriographic features characteristic of aneurysm or tumor may demonstrate the responsible lesion.[7] This technique was not used in any of our patients.

Gastric cooling is an emergency procedure used to control serious bleeding with circulating fluid temperatures of 0° to 20° C employed for prolonged periods of time. Most bleeding stops in 2 hours, but hypothermia is usually maintained for 24 to 72 hours.[8] This method was not used. Iced saline is used routinely for gastric lavage in patients with upper gastrointestinal bleeding to cause local vasoconstriction and decreased bleeding.

About 40 to 50 per cent of patients entering the hospital with massive upper gastrointestinal hemorrhage will require emergency surgery. Those with massive lower bowel bleeding demand emergency surgery less frequently.[2, 9, 10]

We have arbitrarily designated our 3 indications for emergency surgery as (1) uncontrolled rapid bleeding, (2) continuing slow bleeding, and (3) recurrent bleeding. These are defined as follows: (1) uncontrolled rapid bleeding when the patient's condition remains unstable after initial rapid transfusion of 2,500 to 3,000 c.c. of whole blood with evidence of continued bleeding, (2) continuing slow bleeding when the patient has prolonged bleeding requiring more than 500 c.c. of whole blood every 8 hours to maintain stable vital signs and hematocrit, and (3) recurrent bleeding when the hemorrhage restarts after apparently adequate medical treatment and control. Despite these guidelines it must be remembered that evaluation of each patient is essential. Such factors as the presence of associated disease and availability of blood also influence the decision for surgery. Further, operation should be performed sufficiently early in the course of the hemorrhage so that the operation is not that of desperation done as a last resort with the patient in an extremely critical condition.

Generally our indications for elective surgery after upper gastrointestinal hemorrhage has stopped are in patients with a history of ulcer complications and in those with X-ray evidence of gastric ulcer or gastric cancer. In lower intestinal bleeding the indications are less well defined except in patients with cancer or polyps. The decision for elective surgery in patients with diverticulosis depends upon the extent of the disease and history of previous attacks of diverticulitis. Surgery is favored for patients with localized diverticulosis and preceding episodes of diverticulitis.

In emergency operations for upper gastrointestinal bleeding pyloroplasty, truncal vagotomy and ligation of the bleeding point seem to be preferable, especially in patients with duodenal ulcer.[11] The ulcer is sutured even if no bleeding is seen at the time of surgery in order to prevent later hemorrhage. Foster et al[11] reported a mortality of 30 per cent for emergency gastrectomy and only 13 per cent for vagotomy, pyloroplasty, and suture ligation of the ulcer when used in treating massive upper gastrointestinal hemorrhage.

In both bleeding gastric and duodenal ulcers we prefer a procedure in which the ulcer is removed. This is done if it is technically feasible and the patient's condition permits. In gastric ulcer we favor limited partial gastrectomy, while in duodenal ulcer we prefer subtotal gastrectomy or a resectional procedure with vagotomy. We now increasingly use vagotomy, pyloroplasty, and suture ligation of the ulcer in patients with bleeding duodenal ulcer whose clinical condition is very poor.

Blind gastrectomy is to be deplored because of its frequent ineffectiveness. Freeark et al[12] found that of 15 single gastric ulcers responsible for massive bleeding in a series of 77 cases, 7 were located in the proximal third of the stomach and would have remained behind in a standard blind (66 to 75 per cent) subtotal gastrectomy. Blind gastrectomy was used in one of our patients who continued to bleed postoperatively. At autopsy he was found to have esophagogastric lacerations (Mallory-Weiss syndrome).

In 1929 Mallory and Weiss described the syndrome of an alcoholic debauch followed by persistent nausea, vomiting and retching, and massive gastrointestinal hemorrhage. This was found to be caused by longitudinal lacerations of the mucosa and submucosal at the esophagogastric junction. Surgical therapy is used only if conservative management fails. High gastrotomy, adequate exposure of the esophagogastric region, and oversewing the lacerations are performed. The general futility of using the Sengstaken-Blakemore tube and of blind gastric resection in this entity is well established.[13]

When careful exploration with palpation and external visualization of the esophagus, stomach, duodenum, and small and large intestine fails to reveal a source of bleeding, Freeark et al perform a generous gastrotomy and limited duodenotomy to ascertain the source of bleeding. They state that perhaps the greatest single benefit obtained from the use of exploratory gastrotomy (15 cm. or longer) was the identification of esophagogastric lacerations of Mallory-Weiss (11 of 77 cases). One of the characteristic features of this entity found was the presence of subserosal hemorrhage high on the lesser curvature near the esophagogastric junction. This helps to establish the diagnosis before gastrotomy. Deep suture repair controls the bleeding quite well.[12]

One patient developed massive upper gastrointestinal bleeding 6 days after a Whipple pancreatoduodenectomy (including 75 per cent gastric resection) from stress ulcer near the gastric cardia. This was controlled by deep suture ligatures. Beil[14] stated that severe infection in the postoperative period was significant in 74 per cent of patients with stress ulcers. Significant infection was not present in this patient.

The 2 causes of massive lower gastrointestinal hemorrhage among our patients were sigmoid diverticulosis and typhoid fever. The 40-year-old woman with typhoid fever required emergency hemicolectomy for uncontrolled hemorrhage. She died on the fourth postoperative day after receiving a total of 39 units of blood during her 5-day hospital stay.[15] Three patients bled from colonic diverticula. All had diverticulosis of the left half of the colon with maximum involvement of the sigmoid portion. None of these 3 patients required emergency surgery.

Noer et al[16] reported that among 245 patients with gross rectal bleeding diverticulosis was responsible for 70.8 per cent of all massive rectal hemorrhages and that approximately one-fourth of all bleeding from diverticulosis was severe in degree. Cancer of the colon was the most frequent source for mild to moderate bleeding but was unusual for massive hemorrhage.

The statement is often made that black or tarry stools indicate an upper gastrointestinal source. Yet in Noer's series of 245 patients with demonstrated or presumptive evidence of bleeding sources beyond the ligament of Treitz, 55 of the records referred to black or tarry stools. The bleeding in our 4 patients with lower intestinal bleeding was described as dark red, mahogany, or bright red. There were no black or tarry stools.

In the analysis of our 22 cases special attention was given to the following frequently noted errors: (1) inadequate transfusion, (2) failure to operate or improper timing of the operation, (3) avoidable technical surgical complications, and (4) lack of adequate consultation (team approach).

It was commonly observed that little attempt was made to restore the blood volume to normal in these patients. Once the vital signs were stable, even if the hemoglobin was 9 to 10 Gm. and the hematocrit 28 to 32 per cent, further transfusions were unduly delayed. We strongly recommend restoration of normovolemia as quickly as possible being mindful of cardiopulmonary changes that may alter the rate of transfusion in some patients. Often several days elapsed before adequate transfusions had been given. Blood volume studies during acute hemorrhage have been of little value except in cases of chronic bleeding. We favor aggressive transfusion to achieve a hemoglobin and hematocrit of at least 12 to 14 Gm. and 38 to 40 per cent respectively. This affords better oxygenation of tissues and provides an added margin of safety to the patient if rebleeding occurs. Inadequate transfusions were thus noted in 17 of the 22 patients (77 per cent).

Improper timing of operation appeared to be evident in 5 patients (22 per cent). This improper timing was related to undue delay even when the patients had demonstrated continued or recurrent bleeding. Also, the patients' general condition became progressively worse during the period of delay.

Among the 8 patients requiring emergency surgery, only 1 avoidable technical surgical error occurred—the performance of "blind" subtotal gastrectomy in the patient with unrecognized esophagogastric lacerations (Mallory-Weiss syndrome). This patient died as the result of continued hemorrhage. There were no anastomotic leaks.

There was also lack of a consistent team approach. Only 10 of the 22 patients were seen initially and managed jointly by a team (surgeon and internist) and followed by it throughout their hospital course. We believe the absence of this approach accounted for the lack of aggressive transfusion and the delay in surgical management. A team effort is essential if the best results are to be obtained.

Seven of the 22 patients died, producing a mortality rate of 31 per cent. Three of the 14 patients not having emergency surgery died. One died of a presumed coagulation defect. To be of greatest value, clotting studies should be done early and prior to the institution of transfusion therapy if possible. Both patients with esophageal varices died as the result of continued hemorrhage and liver failure. The Sengstaken-Blakemore tube was partially effective in one patient but of no value in the other. Four of the 8 patients having emergency surgery died—2 from continued bleeding and 2 from cardiopulmonary complications. One of these deaths was potentially avoidable—the patient with unrecognized Mallory-Weiss syndrome. Both patients who died from cardiopulmonary problems were elderly (73 and 84 years), had bleeding gastric ulcers, and had experienced 3 episodes of previous hemorrhage. Devitt et al[10] found in a review of 50 consecutive deaths from bleeding peptic ulcer that the natural history of fatal bleeding ulcer was that of multiple recurrent, abrupt, self-limited hemorrhages. The median number of hemorrhages before death was 5, and the median day of death was the fifth after admission. Death seldom occurred in patients under 55 years of age or in the absence of a chronic ulcer. Death appeared to result from inability to compensate for repeated, inadequately corrected blood losses.

## Summary

We have presented 22 patients, 17 males and 5 females, with massive gastrointestinal hemorrhage seen during a 5-year period. Duodenal ulcer was the most common cause of bleeding from the upper gastrointestinal tract while sigmoid diverticulosis was the chief cause of hemorrhage from the lower tract.

The 3 indications for emergency surgery were designated: (1) uncontrolled rapid bleeding, (2) continuing slow bleeding, and (3) recurrent bleeding. It was emphasized that evaluation of each patient is necessary and that emergency surgery should be performed sufficiently early before the patient's condition is grave.

In both gastric and duodenal ulcers we favor a procedure that includes excision of the ulcer. In very poor-risk patients with bleeding duodenal ulcers the operation of vagotomy, pyloroplasty, and suture ligation of the ulcer appears to be the procedure of choice. Blind gastrectomy is to be avoided. Careful search for esophagogastric lacerations (Mallory-Weiss syndrome) and lesions in the proximal stomach is urged.

Aggressive transfusion for early restoration of blood volume and the team approach for optimum care are important for best results.

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# Visualization of Lymphatics During Hysterosalpingography

## Report of a Case

H. C. PRESS, JR., M.D.,* V. K. SAINI, M.B.B.S., M.S.,† AND T. W. DAVIS, M.D.‡

RECENTLY Fisher[1] and Hipona and Ditchek[2] separately described the intravasation of radiographic contrast material into lymphatics during hysterosalpingography. The former reported 2 cases and the latter 1. There is a paucity of information in the literature regarding the visualization of uterine lymphatics during hysterosalpingography, although the above authors cited several European workers who have described this phenomenon. This report records 1 additional case.

### Report of Case

A 45-year-old Negress (FH No. 98-981), gravida III, Para 1, was admitted to Freedmen's Hospital on June 26, 1966 for evaluation of a left adnexal mass which had progressively enlarged over the preceding 2 months. She was known to have several small fibroids. Her menses were regular. The remainder of the clinical history was not remarkable.

Pertinent physical findings were confined to the pelvis. The uterus was slightly nodular and enlarged. The cervix appeared scarred and was difficult to probe. The probing caused severe discomfort. A poorly-defined, firm, nontender mass, measuring approximately 4 cm. in diameter, was palpated in the left adnexa. Laboratory tests were normal.

A hysterosalpingography was performed with injection of 6 c.c. of Renografin-60® into the uterine cavity, during which the patient experienced severe pelvic pain. Roentgenograms (figure 1) taken immediately following the injection revealed contrast material present in lymphatic channels surrounding the uterus. Follow-up films (figure 2) also showed contrast material in the lymphatic drainage from the uterus, as well as in higher presacral and lumbar lymphatics. A total abdominal hysterectomy was performed on June 30, 1966, at which time the adnexal mass was demonstrated to be a pedunculated fibroid.

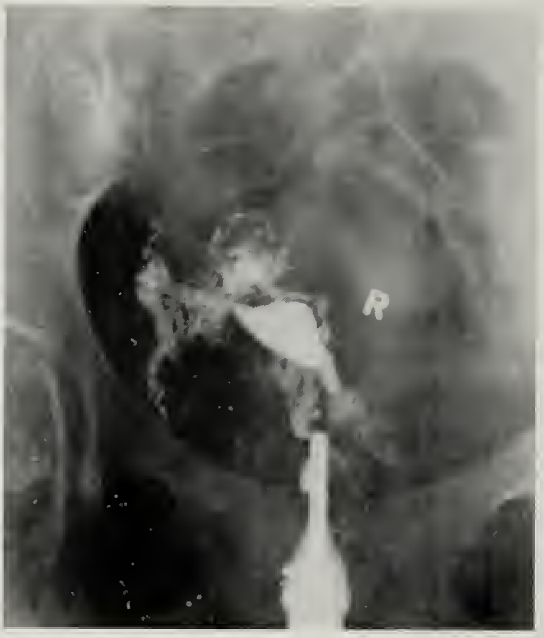

FIG. 1. Film taken immediately following injection of contrast material. Contrast dye is seen in the uterine cavity and in the lymphatics of the uterus and adnexa. Larger lymphatics lying behind the uterus are also shown.

### Discussion

It is known that all the viscera of the body, including the uterus, have rich and intricate networks of lymphatic channels, the patterns being similar to those formed by blood vessels. One of us[3] while studying the blood vessels and lymphatics of the tongue of the rabbit observed clearly visible lymph vessels with tiny tributaries in the subepithelial connective tissue of the papillae of the tongue. These lymphatics accompany the blood vessels, from which they may be identified by differential injection. The lymphatics communicate freely with each other in the lamina propria of the tongue. If the vascular pattern of most viscera is similar it can be assumed that the

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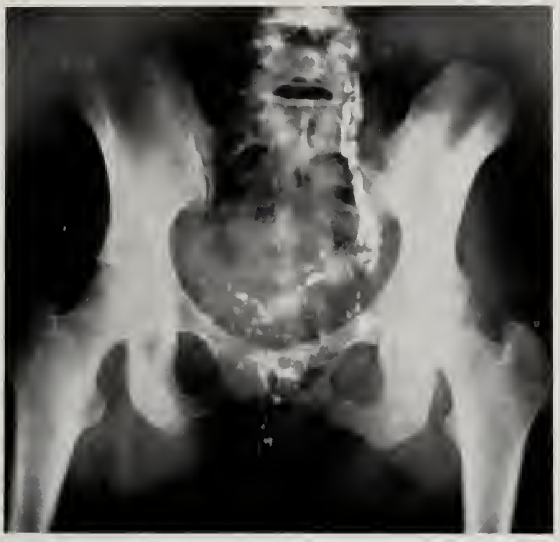

**FIG. 2. Film taken approximately 15 minutes later. The contrast material has passed through the walls of the uterus and has reached the left lumbar lymphatic channels.**

lymphatic pattern of the uterus has a like arrangement, with the tiny lymph capillaries arising immediately beneath the uterine endometrium. Close to the basement membrane these capillaries are supported by delicate connective tissue and soft ground substance.

The flow of Renografin-60 cannot pass through the normal epithelium of the uterine endometrium. It may be assumed, however, that if there is a break or deficiency in the lining membrane of the epithelium, contrast material injected under pressure may make its way into the subepithelial zone, where it could diffuse through the gel-like ground substance and promptly enter the lymphatics.

The lymphatic drainage from the body of the uterus follows 3 principal routes: lumbar, external iliac, and anterior accessory path along the round ligament.[2] Also, it is generally accepted that lymphatics follow the course of the blood vessels, but the exact relationship of the small lymph channels to blood vessels of similar caliber, especially about the uterus, has not been clearly demonstrated. Since the principal blood vessels of the uterus run through the broad ligament, the prompt appearance of contrast material in the presacral and lumbar lymphatics cannot be explained purely on the basis of anatomic facts. There is lymphatic drainage along the uterine and ovarian vessels but, apparently, these are not the only major drainage pathways from the uterus.

It may be noted that in our case, as well as in those cited,[1, 2] there was bilateral obstruction of the fallopian tubes. This undoubtedly causes increase in intra-uterine pressure, facilitating entry of contrast material into the subepithelial zone and into the lymphatics. It is our opinion that bilateral tubal obstruction is a major factor in the intravasation of contrast material into the lymphatics. A second possible major factor is a deficiency in the epithelial lining, since no other demonstrated disease or condition was found to account for this abnormality. Conceivably, any etiologic factor leading to the destruction of the epithelial lining could cause a lymphatic backflow from the uterine cavity into the lymphatic channels.

The 3 previous cases as well as ours occurred in Negro women. This is probably coincidental and does not represent a racial characteristic.

## Summary

A case in which the uterine lymphatics were visualized during hysterosalpingography has been described. The anatomy of lymphatic drainage and possible routes of escape of contrast material from the uterine cavity were discussed. Two possible major factors to produce this occurrence are deficiency or lack of integrity of the epithelial lining and the presence of bilateral tubal obstruction. The fact that the few cases described occur in Negro patients is considered coincidental.

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# Pseudocyst of the Pancreas as a Manifestation of the Battered-child Syndrome

## Report of a Case

TAEK KIM, M.D.,* AND MELVIN E. JENKINS, M.D.†

Fifty-two cases of pseudocyst of the pancreas in childhood have been reported since 1910.[1] Although this condition is relatively rare in children, it follows abdominal trauma frequently enough to be considered in any child with an upper abdominal mass.

The patient in this report demonstrated a pseudocyst of the pancreas following abdominal trauma which was apparently inflicted by the mother. The diagnostic studies which demonstrated the specific lesion will be discussed. Unfortunately, a subsequent accident probably related to maternal abuse resulted in the child's death.

### Report of Case

A 3-year-old boy, who appeared to be somewhat smaller than his stated age, was admitted for evaluation of abdominal pain, vomiting, and drowsiness. According to the mother, the child had fallen down 7 flights of concrete steps several hours before admission. There was no loss of consciousness, although 2 episodes of vomiting occurred shortly after admission.

The birth history was essentially normal. Growth appeared to be slightly retarded, but the neuromuscular development was within normal limits. Uncomplicated mumps was experienced 4 months prior to admission, and he developed chickenpox 5 months before this hospitalization. There was no history of other major illnesses. The patient was the only child of a 19-year-old unmarried mother. The socioeconomic status of the family was at the poverty level. There was no significant history of familial diseases.

The physical examination on admission revealed minimal drowsiness and moderate abdominal pain. There were multiple contusions scattered over the body, especially on the lower extremities. Several scars were present on the scalp and around the neck. The weight was 11 Kg. (below third percentile), the height 92 cm. (at the tenth percentile), and the temperature 99.6°F. The heart rate was 108 per minute, the respiratory rate 28 per minute, and the blood pressure 90/50. The pupils were equal and reacted to light and accommodation. There was no evidence of bleeding about the head and neck. The lungs were normal. The cardiac rhythm was regular, and there were no murmurs. The abdomen was slightly distended, with tympany to percussion. There was moderate tenderness in the lower left quadrant with some muscular guarding but no rigidity. There were no palpable abdominal masses. Neurologic examination was negative. The hemoglobin was 8.8 Gm., with a hematocrit of 28 per cent and white blood cells of 10,700. Roentgenograms of the skull, abdomen, chest and long bones were negative. An intravenous pyelogram was also normal.

In view of the vomiting, abdominal pain and distention, the patient was placed on intravenous fluid during the first 3 hospital days. Although the vital signs remained stable the abdomen appeared to become progressively more distended and there was a tendency toward constipation. On the twelfth hospital day a temperature elevation occurred for the first time and abdominal distention progressed. Except for tenderness in the left upper quadrant and persistent abdominal distention, the boy appeared to be reasonably well for the next 5 days. Because of persistence of symptoms an upper gastrointestinal X-ray examination was done. This revealed a retroperitoneal mass that pushed the stomach anteriorly (figure 1). It was at this point that pseudocyst of the pancreas was first seriously considered. The serum amylase was 394 units (normal 4–25 units/ml.). Serum lipase was 300 units (normal less than 2 units/ml.).

An exploratory laparotomy was performed, which demonstrated a large pancreatic pseudocyst that lay immediately lateral to the greater curvature of the stomach and bulged around the stomach anteriorly. The major organ systems including liver, spleen and kidneys did not show evidence of recent or old injuries. About 500 ml. of fluid was removed from the cyst which contained an amylase level of 181 units and a lipase level of 630 units. A cystogastrostomy was performed to which the patient responded satisfactorily. The serum amylase and lipase remained elevated through the first postoperative month.

On the basis of multiple scars and the pancreatic pseudocyst the possibility of the battered-child syndrome was entertained. Social service investigation of the home environment strongly suggested that the child had been physically abused on several occasions. This suspicion was reported to 2 municipal child protective agencies which conducted further investi-

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gations. However, definite legal proof of physical abuse was not obtained, and on the insistence of the mother the child was discharged to her care after 1 month of hospitalization. There were no legal means through which the child could remain in the hospital without the mother's consent.

Approximately 4 months after discharge the child was admitted to another hospital emergency dispensary "dead on arrival." This admission was only 4 days after a fracture of the arm had been treated at another hospital. Autopsy revealed a skull fracture, acute subdural hematoma, and multiple contusions. The mother explained that the child's injuries had resulted from a fall in the bathtub.

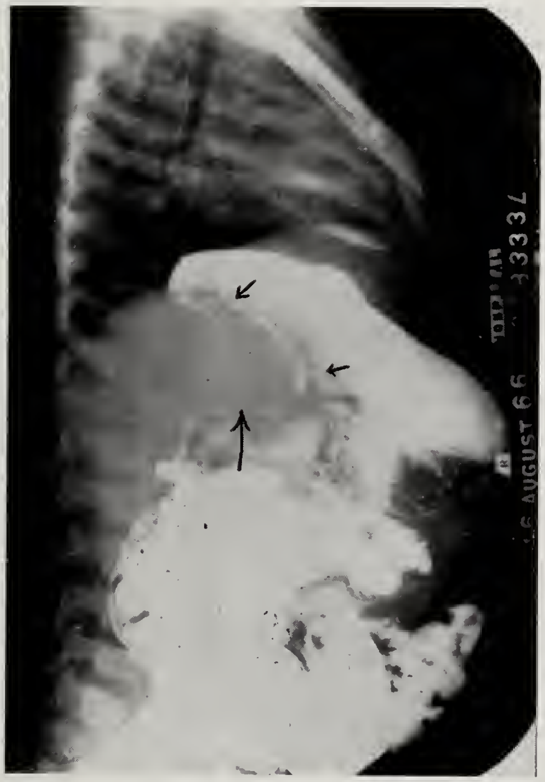

FIG. 1. Large mass pushing the stomach anteriorly and compressing the posterior gastric wall.

## Discussion

Although this patient at times demonstrated most of the signs and symptoms of pseudocyst of the pancreas between his trauma and definitive surgery, the diagnosis was not made until after the characteristic X-ray findings. Characteristic clinical findings in pancreatic pseudocyst are nausea, vomiting, abdominal pain, fever, anorexia, weight loss, abdominal fullness, and a palpable abdominal mass. An abdominal mass in the upper left quadrant was not appreciated in this patient until the day prior to surgery. A palpable abdominal mass has been universally accepted as the most prominent feature on physical examination.[2-5] However, abdominal fullness frequently obscures the mass, and it may not be palpated until it has been outlined on roentgenologic examination.[6] This is especially true in children in whom the possibility of pancreatic pseudocyst is rarely entertained.

Roentgenographic studies are usually needed to establish the diagnosis and to outline the pseudocyst. A flat plate of the abdomen, upper gastrointestinal series, barium enema, and intravenous pyelogram may be required to delineate the mass. Characteristically, the stomach is displaced superiorly and anteriorly, while the transverse colon is displaced inferiorly and anteriorly. The duodenal loop may be widened.

Other laboratory findings are inconsistent. Glycosuria and/or hyperglycemia have been noted in 50 per cent of adults with pancreatic pseudocysts in some series.[6] Our patient had a normal blood glucose. Serum amylase values may be elevated. In the Mayo Clinic Series one-third of the patients had high amylase values.[3] Frank diabetes develops in about 20 per cent of patients with advanced pancreatitis and pseudocyst.[3] This is not a significant problem in children, in whom clinically significant pancreatitis is quite rare.

Our patient was mildly anemic (hemoglobin 8.8 Gm.). It is difficult to determine whether this anemia was related to the pancreatic pseudocyst or whether it was coincidental. Blood loss anemia was encountered in 20 per cent of patients studied by Caravati.[6] Pseudocysts may bleed or be associated with gastric or esophageal hemorrhage. White blood cell counts are of little value, and liver function studies may be normal.

Of considerable concern in our patient was the probability that maternal abuse produced the abdominal trauma which led to the pancreatic pseudocyst formation. About 40 per cent of children treated for blunt trauma to the abdomen have suffered a significant pancreatic injury, and a small percentage of those will go on to develop a pseudocyst of the pancreas.[1] Pseudocyst of the pancreas is a cystic structure located primarily in the lesser sac and its retroperitoneal compartment. Its wall is composed of granulation and fibrous tissue, and the lining is devoid of epithelium. Its boundaries are determined by the organs which outline the lesser sac, and its lumen may or may not communicate with a pancreatic duct.[7] It would appear that inflammation caused by trauma or infection results in the activation of trypsin and lipase which are probably responsible for the digestion of pancreatic and adjacent tissues. Granulation and fibrous tissue proliferation encapsulates the irritating fluid to form the liquid mass within the boundaries of the lesser sac.[8]

Since the abdominal trauma in this child appeared to result from physical abuse by the mother, every effort was made to protect the child through our Social Service Department and local community facilities. The characteristic subperiosteal calcification in children with the chronic "battered-child syndrome" was not seen on X-ray films of the long bones in this child. Altman et al[9] have emphasized that a history of battering in this syndrome is almost never obtained and that one must depend upon indirect evidence. Unfortunately, this means that legal evidence against the adult responsible for the injury is usually circumstantial and therefore presents a weak posture for the prosecution in court. It is difficult to prove maltreatment, since parents can frequently lie effectively when a catastrophe such as a fracture or a brain injury demands an explanation. These parents almost never return to the same hospital after repeated injury. They move from one facility to another where past hospital records are unavailable. In our patient a subsequent fracture of an extremity was treated at another hospital. Four days later he was seen at a third hospital with a fractured skull. As is frequently the case, this mother still could not be prosecuted because the "accidents" were not witnessed by a third party.

The "battered-child syndrome" must be considered as a psychiatric problem in the parent as well as a medical problem in the child.[10] The parent should be considered the prime target for psychiatric assistance. Frequently the father was beaten severely as a child. He therefore identifies himself with the brutality of his own parent and retaliates through his own child. The mother's conflict is more commonly reflected in her jealousy toward a male child. Her hostility toward a male child may be identified with her mother's hatred toward her father.[10] Sometimes the child is regarded as the cause of an unwanted marriage or pregnancy.

More workable guidelines must be developed for laws in the case of the battered child. A spokesman for the Australian Medical Association[11] has suggested that:

1. Physicians should be charged with reporting suspected cases of child abuse immediately to an agency legally responsible for investigating them.
2. Such an agency should have ample resources.
3. Reported cases should be investigated promptly and appropriate services provided for child and family.
4. The child should be protected by an agency, either by continued hospitalization, supervision at home, or removal from home when indicated.
5. The agency should maintain a central registry with provision for removal of a file where, in fact, it is proved that abuse did not occur.
6. The reporting physician or hospital should be granted immunity from any court litigation.

Much remains to be done from a community team approach to cope with the various problems of the battered child and his parents. Local government, the medical profession, and many lay groups must work together not only to publicize the magnitude of the problem but also to design methods to decrease mortality and morbidity.

Pancreatic pseudocysts in children can result from trauma inflicted by adults. Kempe et al[12] have suggested that one should suspect the condition when an abdominal mass is palpated in children thought to be suffering from the "battered-child syndrome."

In regard to the treatment of pancreatic pseudocyst, surgery is performed to facilitate internal drainage. The preferred procedure is cystogastrostomy, which was used in our patient. Surgical excision of the cyst is much less satisfactory than internal drainage.

## Summary

A 3-year-old boy with pseudocyst of the pancreas has been described. This condition is rare in childhood but should be suspected in any child with an abdominal mass following blunt trauma to the abdomen. The clinical features and X-ray diagnosis have been discussed. This case demonstrated the association of pseudocyst of the pancreas and the "battered-child syndrome."

Dr. Roland B. Scott reviewed the manuscript and gave helpful suggestions. Dr. David M. French supervised the surgery. Mrs. Phyllis S. Hathaway gave secretarial assistance.

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(Continued on page 678)

# Incidence of Thalassemia Syndromes and Hemoglobinopathies in a Negro Population*

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THALASSEMIA or Mediterranean anemia was once thought to be a rare condition occurring principally in the peoples of the Mediterranean region such as Italians, Greeks, Syrians, Armenians, etc. The disease is now known to occur in other racial groups, and the present concept is that the condition has a world-wide distribution. Thalassemia has been reported in Negroes from Africa,[1] the West Indies,[2] and the United States.[3,4]

Our interest in this subject began in 1952 with the discovery in our hospital of a Negro boy with thalassemia major.[3,4] Subsequently we encountered additional cases, some in the homozygous state and others existing as the double heterozygous form in combination with sickle-cell hemoglobin. Our first patient is now 17 years of age and is still under observation in our clinic. No doubt many more cases, particularly the milder or asymptomatic forms (thalassemia minor), exist undiagnosed in the general Negro population.

Except for the report of Myerson and his coworkers[5] on the occurrence of thalassemia in 1,000 hospitalized Negro veterans (Veterans Administration Hospital of Philadelphia), few reports have appeared in the medical literature in the United States involving Negroes. The purpose of this study is to establish the incidence of thalassemia and other abnormal hemoglobins in Negroes in the Metropolitan Area of Washington, D. C.

## Method of Study and Results

The patients in the survey comprised 1,506 individuals aged 3 to 17 years selected at random from a pediatric population at Freedmen's Hospital. The initial screening in this group consisted of the following determinations: hemoglobin, hematocrit, red blood cell count, reticulocyte count, and calculation of hematologic indices. In addition, a Wright-stained peripheral blood smear was examined on each child together with a wet sodium metabisulfite preparation for sickling. All children with a positive test for sickling were recalled, together with their parents and siblings for additional studies. The extended testing included hemoglobin electrophoresis on filter paper and starch block, and fetal hemoglobin determination by the alkali denaturation method. When evidence of a hypochromic anemia was found the subjects were also recalled for determination of serum iron levels. Those with low values for serum iron were given a course of iron therapy and reëvaluated by the scheme mentioned above. The results obtained are shown in table 1.

**TABLE 1: Incidence of Hematologic Syndromes Discovered in 1,506 Negro Subjects**

| Syndrome | No. Patients | Incidence (Per cent) |
|---|---|---|
| Thalassemia states: | | |
| Thalassemia minor | 16 | 1.06 |
| High $A_2$ syndrome | 30 | 1.99 |
| Sickle-cell thalassemia | 2 | 0.13 |
| Other conditions: | | |
| Sickle-cell trait | 97 | 6.44 |
| Hemoglobin C trait | 14 | 0.93 |
| Homozygous sickle-cell anemia | 1 | 0.06 |
| Sickle-cell—hemoglobin C disease | 1 | 0.06 |
| Elliptocytosis | 1 | 0.06 |
| Iron deficiency anemia | 72 | 4.78 |

Whenever screening detected hematologic abnormalities in an individual an effort was made

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to study all available members of the family. Table 2 shows the findings in a 5-year-old girl (propositus), her mother, and 2 brothers (family 1). The father was not available for testing. The mother and the 3 children exhibited an elevation in the $A_2$ hemoglobin component (upper limit of normal—3 per cent). The mother, 1 brother 13 years old, and the propositus showed anemia as well as target cells, basophilic stippling, hypochromia, etc. The anemia failed to respond to iron therapy. The 3 siblings were regarded as having thalassemia minor. The heterogeneity of this syndrome is shown in that the 15-year-old brother exhibited a normal peripheral blood smear and no anemia, but his $A_2$ hemoglobin was elevated. The mother had been followed in the adult hematology clinic as a case of thalassemia intermedia.

**TABLE 2: Summary of Hematologic and Biochemical Findings of Family 1**

| Members of Family | Hgb. (Gm.%) | HCT (%) | RBC (million cu. mm.) | MCH ($\mu\mu$g) | MCV ($\mu^3$) | MCHC (%) | Reticulocytes (%) | Sickling of RBC | Paper Electrophoresis (Hgb.) | Fetal Hbg. (%) | $A_2$ Hgb. (%) | Serum Iron ($\mu$g%) | Stained Smear |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Propositus girl, 5 yrs. | 9.5 | 30 | 4.60 | 19.6 | 65.2 | 30 | 1.0 | Negative | A | 0.9 | 7.6 | 90.9 | Anisocytosis and poikilocytosis, polychromasia, hypochromia, basophilic stippling |
| Brother, 13 yrs. | 10.8 | 37 | 4.22 | 25.6 | 87.7 | 29.2 | 0.8 | Negative | A | 2.5 | 6.6 | — | Anisocytosis, target cells |
| Brother, 15 yrs. | 12.4 | 40 | 4.40 | 28.2 | 90.9 | 31 | 0.8 | Negative | A | 0.8 | 6.5 | — | Normal |
| Mother | 10.1 | 35 | 4.70 | 21.5 | 74.5 | 28.8 | 0.4 | Negative | A | 1.8 | 9.0 | — | Hypochromia, anisocytosis, poikilocytosis, target cells, basophilic stippling |

The propositus in family 2 (table 3) was a 7-year-old girl who presented no physical manifestations of a hemolytic anemia. Laboratory studies revealed mild anemia, sickling of erythrocytes, presence of S and F hemoglobin, slight increase in fetal hemoglobin (normal value—less than 2 per cent), target cells, hypochromia, and microcytosis. The mother's blood did not sickle, and only hemoglobin A could be identified on electrophoresis. The father was not available for testing. The propositus was apparently heterozygous for hemoglobins S and F. Ten members of the family showed an increase in the hemoglobin $A_2$ component. One member, C. C., a cousin of the propositus, had a high level of fetal hemoglobin (38.6 per cent) together with hypochromia, microcytosis, target cells, basophilic stippling, and other stigmata of thalassemia.

## Discussion

Traditionally, it has been customary to classify thalassemia as major or minor, depending upon the clinical severity. Generally these 2 types are regarded as representing homozygous and heterozygous states respectively. Sometimes an intermediate variety (hemoglobin 7 to 10 Gm./100 ml.) associated with homozygous, heterozygous, or double heterozygous states is accepted as a clinical entity. Currently most investigators are attempting to classify the thalassemia syndromes on a genetic basis.

The thalassemia syndromes apparently can arise from a variety of genetic aberrations affecting hemoglobin synthesis.[6,7] Beta-globin-chain thalassemia may be characterized as follows:

1. A basic defect in beta-chain synthesis exists.
2. Heterozygote interacts with other beta-chain mutations such as hemoglobins S, C, D, etc.
3. Phenotypes show decreased A and elevated F, $A_2$.
4. Anemia develops after birth.
5. Most common type is seen in the United States.

Alpha-globin-chain thalassemia is characterized by:

1. A basic defect in alpha chain synthesis exists.
2. Heterozygote interacts with other alpha chain mutations such as I, G, D.
3. Phenotypes: hemoglobin Bart or hemoglobin H are present. $A_2$ and F are normal or low.
4. Anemia develops in utero, and in the homozygous state may result in lethal condition of hydrops fetalis.

5. It is particularly common in Southeast Asia, but the incidence may be 2 to 5 per cent in the American Negro.[8]

Other forms of thalassemia-like disorders are hemoglobin Lepore syndrome and hereditary persistence of high fetal hemoglobin syndrome, as well as double heterozygous forms.[8]

**TABLE 3: Summary of Hematologic and Biochemical Findings of Family 2**

| Members of Family | Age (yrs.) | Hgb. (Gm. %) | HCT (%) | RBC (million cu. mm.) | MCH (μμg) | MCV ($\mu^3$) | MCHC (%) | Reticulocytes (%) | Sickling of RBC | Type Hgb. | Fetal Hgb. (%) | $A_2$ Hgb. (%) | Serum Iron (μg%) | Stained Smear |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| V. W., propositus | 7 | 10.1 | 33 | 4.59 | 22.0 | 71.9 | 30.6 | 1.2 | + | SF | 3.3 | — | 92.9 | Hypochromia, microcytosis, target cells, anisocytosis, poikilocytosis |
| C. W., sister | 12 | 12.0 | 41 | 4.79 | 25.1 | 85.6 | 29.2 | 2.5 | – | A | 2.6 | 8.7 | | Normal |
| Y. W., brother | 11 | 10.4 | 36 | 4.51 | 24.1 | 83.5 | 28.8 | 1.7 | – | A | 2.8 | 6.2 | | Hypochromia, target cells, anisocytosis, poikilocytosis |
| B. W., sister | 5 | 10.8 | 36 | 4.16 | 25.9 | 86.5 | 30.0 | 1.0 | – | A | 2.2 | 4.7 | | Normal |
| K. W., brother | 2½ | 10.4 | 36 | 4.12 | 25.2 | 87.3 | 28.8 | 0.8 | – | A | 3.5 | 8.5 | | Anisocytosis |
| D. S., mother | — | 10.8 | 35 | 4.30 | 25.1 | 81.4 | 30.8 | 1.1 | – | A | 1.8 | 5.7 | | Target cells, anisocytosis, poikilocytosis |
| F. L., cousin of propositus | 6 | 10.8 | 34 | 4.31 | 25.1 | 78.9 | 31.7 | 0.5 | – | A | 3.0 | 6.0 | 100 | Hypochromia, anisocytosis, polychromasia, poikilocytosis, target cells, ovalocytes |
| Y. L., mother (sister of D. S.) | — | 12.2 | 23 | 4.52 | 26.9 | 95.1 | 28.3 | 1.3 | – | A | 2.9 | 6.1 | | Anisocytosis, target cell, polychromasia |
| C. C., cousin of propositus | 12 | 10.25 | 36 | 5.15 | 19.9 | 69.9 | 28.4 | 0.9 | – | AF | 38.6 | 5.6 | | Hypochromia, microcytosis, anisocytosis, poikilocytosis, polychromasia, basophilic stippling, target cells |
| S. H., sister of C. C. | 2 | 11.8 | 39 | 4.72 | 25.0 | 82.6 | 30.2 | 1.0 | – | A | 1.5 | 4.8 | | Poikilocytosis, target cells |
| M. C., mother of C. C. (sister of D. S. and Y. L.) | — | 11.8 | 42 | 4.70 | 25.1 | 89.4 | 28.1 | 1.0 | – | A | 3.9 | 6.8 | | Hypochromia, anisocytosis, target cells, polychromasia |

The thalassemia states made up 3.18 per cent of the hematologic disorders discovered in our population sample, whereas the sickle-cell and hemoglobin C hemoglobinopathies constituted 7.62 per cent of the total sample.

Because of the stated occurence of the genes for thalassemia and sickle hemoglobin in Negro populations it is not unusual to encounter individuals bearing heterozygous conditions due to genetic interaction. In this connection, because of the widespread use of filter paper electrophoresis in clinical diagnostic laboratories in hospitals, it is well to reiterate a caution which has been pointed out by Herman and Conley.[9] The following 4 syndromes may give strikingly similar patterns on filter paper electrophoresis:

1. Homozygous sickle-cell anemia.
2. Sickle-cell hemoglobin D disease where a single band forms because hemoglobins S and D have the same electrophoretic mobility.
3. Sickle-cell thalassemia. Certain cases show marked depression of hemoglobin A so that the electrophoretic finding is essentially the single band characteristic of sickle-cell anemia.
4. Simultaneous occurrence of sickling and hereditary persistence of fetal hemoglobin.

Electrophoresis of hemoglobin on agar gels at pH 6 will separate hemoglobins S and D. The examination of parents, siblings, and other close relatives is an important aid for the diagnosis of the other 3 conditions.

(*Continued on page 722*)

# Trends in Neonatal Mortality among Nonwhite Infants in the District of Columbia

## Observations Based on Statistics from Two Local Hospitals

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In 1964 infant mortality in the United States exceeded that in 17 other countries.[1] In this country more than 96 per cent of births were delivered in hospitals in 1960. This pattern continues to be followed at the present time. The purpose of this report is to examine trends in neonatal mortality with emphasis on the nonwhite (essentially Negro) population in the District of Columbia.

Comparative statistics on infant mortality for the District of Columbia and the 50 states for 1963–64 showed that the high rate of 33.5 for Washington, D. C. was exceeded only by Mississippi, whose rate was 40.4. Also, as a municipality, Washington, D. C. had a higher infant mortality than any city in the U.S.A., with a rate of 34.7 in 1964.

Our observations are based mainly upon findings in 2 local institutions, the District of Columbia General Hospital and Freedmen's Hospital. In 1965 approximately 65 per cent of all nonwhite births in the District of Columbia occurred in these hospitals. The D. C. General Hospital is a municipal institution serving the indigent population of Washington, D. C. Freedmen's Hospital is the main teaching facility for the Howard University College of Medicine and over the years has traditionally served a Negro population. The overwhelming majority of patients admitted to the D. C. General Hospital are Negro. Essentially, all patients admitted to the maternity service of D. C. General Hospital are indigent, and about two-thirds of maternity admissions at Freedmen's Hospital are also indigent.

### Observations

The birth rate in the District of Columbia increased to reach a peak in 1961 but has been declining since that time. It will be noted from table 1 that a peak number of births also occurred at the D. C. General Hospital in 1961 and at Freedmen's Hospital in 1963. There has been a decline in births since these years.

**TABLE 1: Number of Live Births at D. C. General and Freedmen's Hospitals for a 10-year Period (1957–1966)***

| Year | D. C. General Hospital | Freedmen's Hospital | Nonwhite D. C. Residents |
|---|---|---|---|
| 1957 | 6,106 | 3,092 | 12,764 |
| 1958 | 6,148 | 3,024 | 12,949 |
| 1959 | 6,559 | 3,048 | 13,501 |
| 1960 | 6,485 | 3,162 | 13,689 |
| 1961 | 6,715 | 3,305 | 14,302 |
| 1962 | 6,392 | 3,338 | 14,224 |
| 1963 | 5,908 | 3,568 | 14,495 |
| 1964 | 6,080 | 3,291 | 14,417 |
| 1965 | 5,948 | 3,057 | 13,948 |
| 1966 | 5,553 | 2,682 | |

* Comparative statistics in tables 1 to 6 are recorded for the fiscal year at the D. C. General Hospital and for the calendar year at Freedmen's Hospital.

The neonatal death rate in the District of Columbia has not changed substantially since 1950. The rate has always been somewhat higher in Negroes. In the past few years this gap has become wider because of a decline in the mortality of white neonates[2] (table 2) with no substantial decrease in the nonwhite rate. The neonatal mortality rates for the D. C. General Hospital, and in the past few years those of Freedmen's Hospital, are substantially higher than the average for the city.

One of the factors undoubtedly influencing the failure to lower Negro neonatal mortality is the increasing incidence of prematurity, as shown by the statistics of the Department of Public Health[2] and those of the 2 hospitals where most of these Negro infants are born (table 3). Overall premature mortality has changed very little since 1950 (table 4). The distribution of premature infants among the various weight groups has remained fairly constant during this time (table 5), and the mortality has not changed much within any one of these weight groups (table 6).

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**TABLE 2: Neonatal Death Rate* per 1,000 Live Births for Residents of D. C. by Color Compared with Neonatal Mortality at D. C. General Hospital and Freedmen's Hospital (1950–1966)**

| Year | D. C. Total | D. C. White | D. C. Nonwhite | D. C. General Hospital | Freedmen's Hospital |
|---|---|---|---|---|---|
| 1950 | 24.5 | 26.0 | 22.6 | 25 | 17 |
| 1951 | 23.3 | 21.4 | 25.5 | 29 | 12 |
| 1952 | 25.2 | 22.7 | 28.0 | 30 | 20 |
| 1953 | 24.0 | 21.0 | 27.1 | 33 | 21 |
| 1954 | 24.7 | 22.9 | 26.4 | 30 | 18 |
| 1955 | 24.7 | 17.4 | 30.2 | 30 | 25 |
| 1956 | 23.9 | 15.7 | 28.9 | 33 | 25 |
| 1957 | 26.0 | 21.3 | 28.5 | 40 | 23 |
| 1958 | 30.0 | 26.0 | 32.0 | 31 | 28 |
| 1959 | 27.2 | 23.4 | 29.0 | 34 | 26 |
| 1960 | 27.0 | 21.5 | 29.4 | 30 | 26 |
| 1961 | 27.0 | 21.3 | 29.4 | 32 | 24 |
| 1962 | 25.9 | 20.6 | 28.0 | 31 | 25 |
| 1963 | 23.9 | 17.2 | 26.4 | 33 | 21 |
| 1964 | 25.9 | 19.2 | 28.1 | 28 | 31 |
| 1965 | 25.1 | 17.6 | 27.0 | 30 | 30 |
| 1966 | | | | 31 | 28 |

* Neonatal period is defined as the first 4 weeks of life.

## Discussion

It is observed that the mortality rates for full-term infants at the 2 hospitals have remained stable over a number of years and are indeed well within accepted limits (table 4). When one compares the incidence of prematurity for the years of 1950 and 1966 for D. C. General Hospital and Freedmen's Hospital the increases are 32 per cent and 44 per cent respectively. While the causes for this significant increase in infants of low birth weight are certainly multifactorial, a dominant consideration is the socioeconomic status of the patients who are served by these hospitals. These institutions share the responsibility for providing a large measure of the maternity services for the economically underprivileged population of the city.

The hazard of neonatal death for infants in the low birth-weight category is shown by the finding that these babies had a mean mortality which was more than 30 times that for full-term infants who were born in the same 2 local hospitals. During a period of observation (1958–1966) the percentage of infants born at the 2 local hospitals in the 1,501–2,000 Gm. weight category (mean 22.9 per cent) was somewhat greater than that which has been reported for the U.S.A. at large (19 per cent).[3] The mean mortality of 11.4 per cent for the infants in this weight class is essentially the same as that reported from the Boston Lying-in Hospital and is considerably lower than the figure reported for the U.S.A. at large (21 per cent).[3]

**TABLE 3: Incidence of Prematurity, Percentage of Live Births (2,500 Gm. or Less) for Residents of D. C., White and Nonwhite, and Comparable Figures from D. C. General Hospital and Freedmen's Hospital for the Period 1950 to 1966**

| Year | Total D. C. | White D. C. | Nonwhite D. C. | D. C. General Hospital | Freedmen's Hospital |
|---|---|---|---|---|---|
| 1950 | 12.2 | 10.4 | 14.4 | 12.8 | 10.2 |
| 1951 | | | | 12.6 | 9.4 |
| 1952 | | | | 13.6 | 10.7 |
| 1953 | | | | 14.3 | 9.9 |
| 1954 | | | | 14.2 | 10.8 |
| 1955 | | | | 15.4 | 11.5 |
| 1956 | | | | 19.0 | 10.7 |
| 1957 | 12.0 | 8.0 | 14.2 | 16.0 | 11.0 |
| 1958 | 12.3 | 8.5 | 14.2 | 16.4 | 10.9 |
| 1959 | 12.5 | 8.7 | 14.3 | 17.1 | 13.2 |
| 1960 | 12.4 | 7.9 | 14.4 | 16.1 | 12.4 |
| 1961 | 12.5 | 8.9 | 14.0 | 16.0 | 13.4 |
| 1962 | 12.4 | 8.3 | 14.1 | 16.2 | 12.4 |
| 1963 | | | | 17.6 | 12.5 |
| 1964 | | 8.3 | 14.2 | 16.6 | 13.8 |
| 1965 | | 7.8 | 14.0 | 16.7 | 15.0 |
| 1966 | | | | 16.8 | 14.6 |

**TABLE 4: Premature and Full-term Mortality (Per cent) at D. C. General Hospital and Freedmen's Hospital (1950–1966)**

| Year | Premature | | Full-term | |
|---|---|---|---|---|
| | D. C. General | Freedmen's | D. C. General | Freedmen's |
| 1950 | 16.1 | 12.0 | 0.5 | 0.6 |
| 1951 | 17.3 | 11.0 | 0.7 | 0.2 |
| 1952 | 17.3 | 15.0 | 0.7 | 0.3 |
| 1953 | 18.4 | 19.0 | 0.5 | 0.5 |
| 1954 | 18.5 | 16.0 | 0.3 | 0.3 |
| 1955 | 17.7 | 19.0 | 0.3 | 0.2 |
| 1956 | 16.4 | 22.0 | 0.4 | 0.4 |
| 1957 | 15.9 | 17.0 | 0.4 | 0.8 |
| 1958 | 16.5 | 21.8 | 0.5 | 0.4 |
| 1959 | 17.3 | 16.1 | 0.3 | 0.5 |
| 1960 | 16.3 | 18.8 | 0.3 | 0.4 |
| 1961 | 17.1 | 15.6 | 0.5 | 0.3 |
| 1962 | 17.6 | 16.3 | 0.1 | 0.5 |
| 1963 | 17.6 | 14.9 | 0.2 | 0.3 |
| 1964 | 15.0 | 19.2 | 0.4 | 0.5 |
| 1965 | 15.0 | 17.6 | 0.4 | 0.4 |
| 1966 | 15.0 | 18.0 | 0.8 | 0.2 |

Traditionally, race has been regarded as a significant factor in studies dealing with both infant and maternal mortality in this country. However, when one focuses upon remedial measures it is more fruitful to regard the white-nonwhite mortality differentials as primarily socioeconomic in nature rather than racial per se. The economic deprivation of the nonwhite population is reflected in lower median income and education levels, a higher rate of unemployment, and dependence upon substandard housing and living conditions, particularly in the large urban areas.[1] In the United States the nonwhite population consists of approximately 90 per cent Negro and 10 per cent other races. The significant differential in infant mortality between whites and nonwhites is shown in the reported rates of 22.3 and 41.7 respectively for the 2 groups in the U.S.A. for 1963.[4] During the same period the rates for white-nonwhite populations in the District of Columbia were 24.0 and 37.1 respectively.

**TABLE 5: Percentage of Premature Infants in Various Weight Groups at the Two Hospitals (1958–1966)**

D. C. General Hospital

| Weights | 1958 | 1959 | 1960 | 1961 | 1962 | 1963 | 1964 | 1965 | 1966 |
|---|---|---|---|---|---|---|---|---|---|
| 0–1,000 Gm. | 8.3 | 10.6 | 9.5 | 9.4 | 10.1 | 10.7 | 9.2 | 8.3 | 8.8 |
| 1,001–1,500 Gm. | 11.4 | 10.0 | 9.3 | 11.8 | 11.6 | 10.0 | 8.3 | 11.6 | 9.7 |
| 1,501–2,000 Gm. | 20.8 | 23.2 | 18.0 | 18.5 | 21.1 | 20.0 | 22.0 | 20.9 | 19.5 |
| 2,001–2,500 Gm. | 59.5 | 56.2 | 63.2 | 60.3 | 57.2 | 59.3 | 60.5 | 59.2 | 62.0 |

Freedmen's Hospital

| Weights | 1958 | 1959 | 1960 | 1961 | 1962 | 1963 | 1964 | 1965 | 1966 |
|---|---|---|---|---|---|---|---|---|---|
| 0–1,000 Gm. | 12.4 | 10.4 | 10.3 | 10.4 | 10.1 | 7.7 | 10.3 | 8.3 | 9.4 |
| 1,001–1,500 Gm. | 12.7 | 12.2 | 14.1 | 11.8 | 9.6 | 9.5 | 11.4 | 11.0 | 9.9 |
| 1,501–2,000 Gm. | 21.3 | 18.6 | 19.5 | 24.9 | 20.4 | 21.1 | 18.2 | 21.4 | 23.7 |
| 2,001–2,500 Gm. | 53.6 | 58.8 | 56.1 | 52.9 | 59.9 | 61.7 | 59.9 | 59.2 | 57.0 |

Harper[5] stated that "deaths among low birthweight infants now comprise one-third of all infant deaths and one-half of all neonatal deaths." It is therefore worthwhile to focus attention on this category even though the true cause of premature births can be medically confirmed in only about half of the cases. It has been established that control on the incidence of premature births can be favorably influenced by attention to the following factors:

1. Early, adequate and regular prenatal care for the mother. This includes appropriate nutritional supplementation, early diagnosis, and treatment of acute and chronic maternal disease such as infectious disease, preëclampsia, chronic hypertension, diabetes mellitus, heart disease, sickle-cell anemia, etc. A significant number of

**TABLE 6: Per cent Mortality of Premature Infants by Weight Groups at the Two Hospitals (1958–1966)**

D. C. General Hospital

| Weights | 1958 | 1959 | 1960 | 1961 | 1962 | 1963 | 1964 | 1965 | 1966 |
|---|---|---|---|---|---|---|---|---|---|
| 0–1,000 Gm. | 91.5 | 97 | 92 | 93 | 91 | 92 | 93.6 | 96 | 89 |
| 1,001–1,500 Gm. | 43 | 41 | 37 | 41.7 | 51.6 | 43 | 36.1 | 40 | 22 |
| 1,501–2,000 Gm. | 11 | 10 | 16.4 | 14.1 | 27.2 | 9 | 10 | 8 | 9 |
| 2,001–2,500 Gm. | 2.7 | 1.0 | 1.2 | 1.8 | 7.1 | 3 | 1.6 | 1.0 | 0.6 |

Freedmen's Hospital

| Weights | 1958 | 1959 | 1960 | 1961 | 1962 | 1963 | 1964 | 1965 | 1966 |
|---|---|---|---|---|---|---|---|---|---|
| 0–1,000 Gm. | 97 | 73.8 | 90.7 | 71.1 | 90.5 | 82.8 | 98.3 | 97.3 | 94.5 |
| 1,001–1,500 Gm. | 45 | 57.1 | 43.6 | 36.5 | 42.5 | 54.7 | 53.9 | 43.1 | 43.5 |
| 1,501–2,000 Gm. | 14 | 9.3 | 9.2 | 11.8 | 10.5 | 8.5 | 7.2 | 15.1 | 13.9 |
| 2,001–2,500 Gm. | 1.7 | 1.3 | 3.7 | 2.1 | 1.6 | 2.5 | 2.6 | 2.6 | 2.6 |

women whose infants were delivered at the 2 local hospitals involved in this study have not received adequate prenatal medical care. In many instances this is due to failure of the patient to seek and use existing health facilities. Apparently new and more imaginative educational devices are needed in order to reach and motivate this particular segment of the population.

2. Early diagnosis of multiple pregnancy and institution of a rest program in the last trimester may circumvent a premature labor.

3. Premature rupture of fetal membranes is said to occur more commonly in the presence of nutritional deficiency.[6] Multivitamins, iron, and protein supplements are of critical importance.

4. The use of anti-Rh gamma globulin shows promise of controlling Rh iso-immunization.

5. Other factors which have been associated with low birth weight are teenage pregnancy, low blood volume and small heart size, cigarette smoking, etc.

6. Within recent years pediatricians, obstetricians, anesthesiologists, and surgeons have focused increased attention upon efforts to improve the survival of all newly born infants including the premature. Recent innovations include improved methods of resuscitation; intra-uterine blood transfusions; control of nursery infections, particularly staphylococcal; early feeding to combat neonatal hypoglycemia in the premature; better microchemical techniques which provide improved controls for parenteral fluid therapy; early identification of high-risk infants; institution of intensive care units for the newly born in distress; early diagnosis and corrective surgery, particularly for conditions in the alimentary canal, respiratory tract, cardiovascular system, genitourinary tract, and central nervous system; early recognition and treatment of genetic and metabolic disorders which could lead to death or mental retardation, etc.

7. Perinatal mortality conferences provide an opportunity for continued education of the staff and the development of preventive measures and serve as a vehicle for better communications between pediatricians, obstetricians, nurses, pathologists, and other members of the team.

8. Adequate nursing service from the standpoint of quality and quantity is invaluable for the early care of low birth-weight infants.

9. The pediatrician and obstetrician in particular must continue to seek better means to identify the ingredients of the heterogeneity which characterizes infants who fall in the category of low birthweight. Progress has already been made in separating "true" prematurity from postmaturity. Infants who fall in the latter category may also exhibit low birth weight.

10. Hospital administrators and health officers can contribute to the control of prematurity and infant mortality by providing adequate facilities for maternal and child care in outpatient clinics and indoor hospital services.

11. Medical schools and Federal, state and private organizations should continue to provide funds for research in this critical area.

12. In our opinion, the current status of infant mortality in the District of Columbia is of sufficient magnitude and importance to the community to warrant the holding of a city-wide conference for a discussion of the many facets of this major public health problem in an effort to evolve remedial recommendations and control measures.

## Summary

Neonatal statistics from the D. C. General Hospital and Freedmen's Hospital show a decline in the total number of births since 1961, increasing incidence of premature births since 1950, particularly evident at Freedmen's Hospital, and no substantial change in neonatal mortality since 1950.

About 65 per cent of all nonwhite births in the District of Columbia take place in these 2 institutions. They share the burden of providing obstetrical and neonatal care for a large portion of the socioeconomically underprivileged population in this city.

Remedial measures have been suggested with emphasis on controlling the mounting incidence of premature births.

Dr. Paul B. Cornely provided helpful suggestions in the preparation of this manuscript.

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(*Continued on page 678*)

# The Role of Radio in Health Education of the Public

**M. Y. HESHMAT, M.D., D.P.H.***

THIS SUBJECT will be discussed with reference to an educational program conducted in Washington, D. C., where 60 talks on a variety of health topics were broadcast over a period of 4 months.

## History and Trends

The United States Public Health Service pioneered the use of radio for health education of the public when it put on the air its first health message in July 1921. That first message grew into a series of 2 15-minute programs each week. The unusual character of this radio service, the first of its kind, created such widespread interest that by 1924 48 radio stations were carrying the series, and health education radio was really launched.

Among all state departments of health, that of New York City took the lead when it started to broadcast its first health series in March 1922.[1]

The American Medical Association began its own series as early as 1925, on the NBC network. By the end of the first decade of radio many official voluntary health and medical organizations, both national and state, were already passing electrical transcriptions from their own series, as well as program ideas, to their local affiliated groups. The use of radio for health education continued to flourish in the 1930's and '40's. In 1949, for example, more than 10,000 local broadcasts were made from the AMA electrical transcriptions alone. At the same time the AMA was broadcasting weekly health programs on 3 national networks.[2,3]

The early health broadcasts were too 'talky,' overloaded with technical words, and not in keeping with the best radio techniques. During its second decade the health broadcast developed enormously as health agencies started to use radio artists and talented, famous radio personalities. Emphasis shifted from straight talks to a variety of presentations, e. g., interviews with outstanding authorities, dramatizations with summaries by medical specialists, musical interludes with interspersed information, first-person documentaries, group forums, etc.

The 1950's witnessed great changes in broadcasting.

First, there was the television boom of the early 50's and the simultaneous springing up of large numbers of independent local radio stations. This resulted in a rapid loss of popularity of health broadcasts on national networks. In fact, the AMA had to discontinue all its network programs in 1955.

Second, radio stations started to devote more time to news, music, and sports, with a strong tendency toward brevity. Consequently, the 15- and 30-minute health broadcasts became no longer suitable and were gradually replaced by spot announcements of 20 seconds to a few minutes each. Coincident with these changes, radio was used more and more for short announcements concerning various phases of local health drives for mass screening or vaccination. Unfortunately, this has been at the expense of programs primarily devoted to education of the masses, which had shrunk to a significant degree.[2–7]

Is radio losing prestige as a medium for public health education? Are we overlooking the fact that there are 250 million radio sets in the USA, more than 1 set for every person, and that 85 million Americans listen daily to radio?[8]

Interest in evaluating the effectiveness of radio in health education has always been meager. One of the earliest attempts in this respect was that which was made by the New York Academy of Medicine when it analyzed more than 30,000 communications received in response to a series broadcast in the period between 1935 and 1939. The authors concluded that the number of communications received following any radio talk was no criterion either of the size of its audience or of its effect. More recent literature shows that the evaluation of the educational role of radio is still lagging. In fact, most of the published data in this area in the past 15 years has been limited to incidents where radio was used with several other media in promoting local health drives and where

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planners limited themselves to seeking the answer as to how many people were reached by radio compared to the number reached by other media. Very few authors conducted controlled field experiments for the purpose of evaluating the role of radio. Radio was used with other media, and its role could not be adequately measured.[9–12]

### The Impact of WOOK/Howard University Health Broadcasts on a Poor Negro Community

The Department of Preventive Medicine and Public Health of Howard University College of Medicine and WOOK Radio Station in Washington, D. C. conducted an educational program in the period between December 4, 1964 and April 2, 1965. Staff members of the department gave a total of 60 talks on a variety of health problems on the radio during that period. Each talk was of 2 minutes' duration and was repeated 3 or 4 times daily, and each day carried a new message. The following subjects were discussed: cancer, heart disease, diphtheria, diseases of children, whooping cough, tetanus, smallpox, streptococcal infections, prenatal care, dental health, tuberculosis, venereal diseases, food poisoning, food and nutrition, and housing and health. At the termination of the series a study was conducted for the purpose of measuring the effect of such an intensive educational program on the knowledge, attitudes and behavior of the residents of one of the low-income sections of Washington, D. C. exclusively.

### Methodology

The study was based on a questionnaire interview by a representative sample of the residents of Census Tract 49 in the City. The area contained 2,955 households. The median family income was $3,474, and the median school years completed was 8.0.

A preliminary household census was conducted before drawing the sample to be studied. Households were numbered in sequence, and every tenth household was included in the sample. One adult member in each household in the sample was interviewed.

The questionnaire form contained 28 questions, most of which required only a 1-word answer. Questions were so formulated as to furnish data on age, sex, occupation, education, income variables of attention, interest and absorption, and changes in attitudes and behavior patterns. The questions were tested prior to this on a similar group to insure clarity and to determine the general applicability and comprehensiveness of the questions.

The interviewing was conducted over a period of 3 weeks, starting 1 week after termination of the program. The task was undertaken by 3 persons well trained in interviewing techniques, all of whom had received 4 hours of training, with weekly conferences being held to discuss any difficulties they might have encountered and to insure that acceptable procedures were followed.

The interviewers completed 282 questionnaires, with 17 rejections because of the questionable validity of responses, which reduced the number acceptable to 265 respondents. In the group there were 123 males and 142 females (241 Negroes, 21 Caucasians, and 3 of other races). As for education, 98 respondents had finished 8 years or less of elementary school; 148 finished from 1 to 4 years of high school; 18 finished 1 or more years of college, and 1 was not noted. One hundred and five respondents had family incomes under $2,000; 126 earned from $2,000 to $4,000; 32 earned from $5,000 to $9,999; and 2 did not indicate their income.

### Results

The listening patterns of groups of respondents on various levels of education and income were studied; the percentage of respondents and number of daily listening hours by education and family income are recorded in table 1.

**TABLE 1: Percentage of Respondents and Number of Daily Listening Hours by Education and Family Income**

| Education and Family Income | Less Than 1 Hour | 1 to 3 Hours | More Than 3 Hours | No Answer |
|---|---|---|---|---|
| Education: | | | | |
| 8 elementary or less | 10.2 | 29.6 | 55.1 | 5.1 |
| 1 to 4 yrs. high school | 16.2 | 32.5 | 43.2 | 8.1 |
| 1 or more yrs. college | 16.7 | 50.0 | 16.7 | 16.6 |
| Family Income: | | | | |
| Under $2,000 | 16.2 | 21.9 | 56.2 | 5.7 |
| $2,000–$4,000 | 11.9 | 34.1 | 43.7 | 10.3 |
| $5,000–$9,999 | 15.6 | 62.5 | 21.9 | — |
| TOTAL | 14.0 | 32.4 | 45.7 | 7.9 |

In spite of the fact that 60 health messages were broadcast during the campaign, 36.2 per cent of respondents missed them altogether. Males heard more topics than females did. While age was not a major factor in determining the number of topics heard, family income and education were significant factors, as shown in table 2.

The data in tables 1 and 2 indicate that the higher the respondents' educational status, the less hours they listen to radio daily but the more health programs they hear. This proves that education definitely increases interest in health talks. Also, respondents with family incomes from $2,000 to $4,999 heard more health messages than any other group. The fact that this group heard slightly more topics than the higher income group may be explained by their longer daily listening to the radio.

**TABLE 2: Percentage of Respondents and Number of Health Topics Heard by Education and Family Income**

| Education and Family Income | None | 1 Topic | 2 to 3 Topics | 4 Topics or More | No Answer |
|---|---|---|---|---|---|
| Education: | | | | | |
| 8 yrs. elementary or less | 37.8 | 25.5 | 16.3 | 7.1 | 13.3 |
| 1 to 4 yrs. high school | 37.8 | 31.1 | 19.6 | 8.1 | 3.4 |
| 1 or more yrs. college | 16.7 | 33.3 | 27.8 | 16.7 | 5.5 |
| Family Income: | | | | | |
| Under $2,000 | 41.0 | 25.7 | 19.0 | 6.7 | 7.6 |
| $2,000–$4,000 | 33.3 | 32.5 | 19.9 | 9.5 | 4.8 |
| $5,000–$9,999 | 34.4 | 28.1 | 15.6 | 9.4 | 12.5 |
| TOTAL | 36.2 | 29.1 | 18.9 | 8.3 | 7.5 |

As for the amount of information retained by respondents, it was found that 36.2 per cent did not recall hearing any health talk on WOOK, 54.1 per cent recalled less than 2 per cent of what was presented, 6.0 per cent recalled 2.3 per cent, and only 2 per cent recalled more than that. Again, the higher the educational level of respondents, the more health information they retained.*

In order to measure the respondent's interest in various health subjects we asked women whether they were pregnant and asked all respondents if they had children under 12 years of age, and whether they or any member of their immediate family were suffering from cancer, heart disease, or tuberculosis. These questions located the respondents who possibly needed the information on these subjects. The results are presented in table 3.

**TABLE 3: Number and Percentage of Respondents Who Heard Health Topics in the Total Sample and among Those Who Needed the Information**

| Health Topics | No. Respondents Who Needed the Information | No. and Per cent of Respondents Who Heard Information | | | |
|---|---|---|---|---|---|
| | | In the Sample | | Among Those Who Needed It | |
| | | No. | Per cent | No. | Per cent |
| Cancer | 9 | 23 | 8.7 | 5 | 55.5 |
| Heart disease | 31 | 32 | 12.0 | 18 | 58.1 |
| Tuberculosis | 9 | 14 | 5.3 | 4 | 44.4 |
| Prenatal care | 11 | 13 | 4.9 | 3 | 27.3 |
| Childhood diseases | 91 | 42 | 15.8 | 29 | 31.9 |

It is evident from the data presented in table 3 that interest plays an outstanding role in the success of communication. In the case of cancer, for example, the message reached 6 times more respondents among those who needed the information than among members of the sample in general.

Moreover, it was found that messages discussing heart attacks, cancer and other diseases affecting mainly the old reached more respondents among those of 50 years of age or older than among younger age groups. Talks on venereal diseases reached many more teenagers and respondents in the 20–29 age group than among older members of the sample.

When the respondents were asked to indicate how much their attitudes and behavior were affected by what they had heard, 5.7 per cent of them indicated that they were more concerned about their health, as a consequence, or started to think "a lot" about their health. Three per cent said that they became convinced about the importance of seeking medical care early. As for behavioral changes, 3.5 per cent of those who heard the program actually visited private doctors or clinics for chest X-ray films or check-ups, while 1.3 per cent took more care in choosing foods for their children, 0.3 per cent allowed their children to take "shots" at school, and 0.4 per cent paid more attention to preventing accidents at their homes.

## Discussion

Why did more than one-third of the population miss our program altogether, and why did the majority of those who came across the program retain less than 2 per cent of what was presented? Was it because radio had lost ground as a medium for health education, or were there factors peculiar to the situation which undermined the effectiveness of the program?

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* These data were based on the fact that the average health talk emphasized 5 health points, and the total program carried about 300 of such points. As there was no pre-measure, it was impossible to determine whether health knowledge the respondents claimed to have learned from our program was really gained from it, or some information was known to them beforehand. Many respondents, however, gave the health facts in the same order and way they were broadcast, and 5 per cent recalled names of physicians presenting the health topics in question.

In following through this exploration we shall attempt to answer these questions in the context of some concepts and empirical data from the field of mass communication.

Communication research indicates that information and events delivered via mass media, even those widely publicized, do not reach all their intended audience. In every community there are people who constantly tend to be less aware of publicized events and news. Hyman and Sheastley[13] spoke of them as the "hard core of chronic know-nothings."

Moreover, among people of the same socioeconomic and educational level there are individuals who expose themselves to mass media more than others. They are the "gate keepers" or "opinion leaders" who transmit what they absorb from mass media to the "inert," less active members of the community.[13,14]

Research studies in many parts of the world have shown that the low-income and less educated sections of the population expose themselves less to radio programs discussing serious material such as public affairs, politics, and educational programs than others do. The study discussed in this paper was conducted in one of the low-income sections of the city. Thus there is reason to believe that its impact on the population as a whole was greater than on residents of the census tract surveyed.[15,16]

The saying, "Radio is everywhere at all times," may be true in a very broad sense, but, as far as a particular program is concerned, it is certainly not valid. Our program was available only on one channel of the radio dial and at a time determined by the radio station, not by the listener. Less than one-third of respondents mentioned WOOK as their favorite station. Those who habitually listen to stations other than WOOK missed the program altogether. As for the timing, the talks were squeezed in whenever there was air time to fill, irrespective of the nature of the health message and the time its intended audience most probably would tune in. Those who were accustomed to listening to radio less than 1 hour a day (14 per cent of the respondents) had little chance to catch the message. Experts on educational radio emphasize careful systematic promotion of educational programs to attract and build up audience-listening.

All available media (letters, posters, newspapers, television and other radio stations, etc.) should be used to announce subject and time of the program. All possible means which could command attention should be used in the announcements. The program discussed in this paper neglected this aspect of promotion entirely. In fact, when respondents were asked what to recommend to make future programs more successful 11.8 per cent advised broadcasting the talks at fixed times of the day and notice of those times in advance.

The simple fact that our program had education as its major purpose prevented it from gathering mass attention. Commercial radio programs devoted primarily to amusement of the listeners demand no more than an acquiescing attention, whereas educational programs require active participation. Everyone likes to be entertained and amused, but only those who are willing to be instructed lend themselves to the process. The person's decision to continue to listen to a health message, once it captures his attention, depends upon his interest in the information it carries. It is impossible to produce an educational program that will appeal to all people who happen to be listening. In our program, for example, there were certain messages which reached 8 times more respondents among certain groups than among members of the sample in general. Thus educational programs, by nature, do not reach and influence large masses of people.

The program described here was broadcast in the form of straight talks rather than more attractive and varied forms of presentation.

Experts indicate that educational programs should not be cluttered with too much material but geared to emphasize a few points that could be remembered by the listeners. The health talks in the program under discussion contained much more material than the average listener in the census tract surveyed could grasp and absorb; e. g., there were 5 broadcasts on heart disease emphasizing more than 30 health facts. The program, furthermore, was broadcast over a period of 4 months, and the survey was conducted after its termination. This aggravated the problem of memory on the part of the respondents. In fact, it was evident that health topics discussed in the latter part of the program were mentioned more by respondents than those presented in the first few weeks of its operation.

## Summary

Historically, the medical profession was among the early users of radio for education of the public. During its first 3 decades radio was used extensively for health education. Series of 15- to 30-minute programs were popular, and various attractive ways of presentation were used. From the late 50's on, spot announcements became more and more popular and gradually replaced the long educational programs. Also, radio has been used mostly for advertising local health drives rather than primarily for education.

A survey to determine the impact of an educational program conducted by Howard University College of Medicine on a low-income section in Washington, D. C. has been described. The survey data were presented as a matrix for discussing the role of radio in health education. Of the sample interviewed 36.2 per cent missed the program altogether, and the majority of those who heard it did not recall more than 2 per cent of what was presented. Possible factors resulting in this low effect were:

1. Educational programs, in general, do not attract mass audiences.

2. The impact of the program was measured among a group known to have less interest in serious radio programs.

3. No promotional activities were undertaken to attract and build an audience for the program.

4. The program was presented in the form of straight talks, carrying much more information than the average audience could grasp.

5. The interviews were conducted at the termination of the program which stretched over a period of 4 months. This fact augmented the problem of memory on the part of respondents and certainly limited the amount of health information they could remember.

The need for evaluation of the present role of radio in health education has been indicated. There is also a need for controlled studies to guide us to the best ways to conduct health education programs on the radio, including optimal duration and most suitable methods of presentation of health broadcasts.

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# Allergy in Negro Children

## II. Incidence in Two Population Groups in Washington, D. C.

M. NICK SHERRY, M.D.,* AND ROLAND B. SCOTT, M.D.†

In 1934 Vaughn[1] stated that 10 per cent of the population in the United States suffered from frank allergy sufficiently severe to require medical attention. In 1961 Appel, Szanton and Rapaport[2] reported an incidence of 23.7 per cent in a pediatric group of 6,036 individuals. On the basis of 1,842 questionnaires completed by parents of school children (ages 5 to 15 years), Arbeiter[3] found that 24.1 per cent of the youngsters had major allergic disorders.

Crook and his co-workers[4] reported that 14 per cent of 1,225 children observed in a private group practice exhibited clear-cut major allergies. An earlier report by London[5] (1937) disclosed an incidence of 6.6 per cent allergic disorders in 1,500 patients seen consecutively in his pediatric practice.

Appel's group investigated pediatric populations in New York State, Connecticut and Montreal, while Arbeiter's study was performed in a Chicago suburb (Munster, Indiana). Crook's patients lived in the vicinity of Jackson, Tennessee, and London's study was done in Durham, N. C. All of these surveys and studies were carried out in predominately Caucasian populations. Our study is unique in that it is based on observations on Negro infants and children.

### Method of Study and Results

The children in this study comprised 2 groups. Group 1 consisted of 1,565 individuals who ranged in age from infancy to 15 years. They were observed by pediatricians who were engaged in general private practice. The incidence of major allergic disorders in this group was 10.5 per cent with the following symptom distribution (table 1).

**TABLE 1: Incidence of Allergic Disorders from Infancy to 15 Years of Age**

| Disorder | No. Cases | Per cent of Total |
|---|---|---|
| Bronchial asthma | 74 | 4.7 |
| Allergic eczema | 41 | 3.0 |
| Allergic rhinitis | 35 | 2.2 |
| Urticaria | 8 | 0.5 |
| Cow's milk allergy | 2 | 0.12 |

Group 2 consisted of 666 school children ranging in age from 6 to 14 years. There were 280 males and 386 females. All of these children were born on the east coast of the United States. The study was conducted by the use of questionnaires which were completed by parents with the aid of written instructions supplied by the authors. A total of 131 or 16.6 per cent of the children in this group were reported to exhibit major or minor allergies. The symptom distribution is shown in table 2.

**TABLE 2: Incidence of Allergic Disorders in Children Aged 6 to 14 Years**

| Disorder | No. Cases | Per cent of Total |
|---|---|---|
| Bronchial asthma | 42 | 6.3 |
| Allergic rhinitis | 30 | 4.5 |
| Allergic eczema | 17 | 2.5 |
| Urticaria | 11 | 1.6 |
| Other allergies (drug, food, insect sensitivity) | 31 | 4.6 |

### Discussion

Bronchial asthma was the most frequently observed allergic disorder in groups 1 and 2. The inclusion of infants in group 1 no doubt explains why allergic eczema occupied second place in occurrence in this group whereas allergic rhinitis held second place in group 2 where the children were all of school age. In a previous study we[6] pointed out the similarity in distribution of clinical types of allergy in Negro and Caucasian allergic children based upon organ involvement. In children of both races asthma, eczema, and allergic rhinitis were the most frequently reported allergic syndromes.

The higher incidence of allergy in the second group is attributed to a relatively higher percentage of older children of school age who experienced a correspondingly wider and longer exposure to allergens.

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Because of differences in geographic location and variations in method of study it is often difficult to make a meaningful comparison of results reported in the literature on the incidence of allergic disorders by different investigators . However, certain similarities between Arbeiter's survey of children aged 5 to 15 years who lived in an upper middle-class income suburb (Indiana) with the school children (ages 6 to 14 years) in group 2 of our study exist. Both studies were conducted by the use of questionnaires. Arbeiter's series involved the analysis of 1,842 questionnaires, whereas only 666 children were in group 2 of our study. The incidence of asthma and eczema in Arbeiter's study was 4.9 per cent and 4.4 per cent respectively. Comparative results for the children in group 2 of our study were 6.3 per cent and 2.5 per cent respectively for these 2 major allergies. The most striking difference in distribution occurred in allergic rhinitis in which the incidence was 14.8 per cent in his series and 4.5 per cent in our group. This significant difference may be attributed to a lower natural occurrence of allergic rhinitis in Negro children[6] as well as aggravation of nasal (hay fever) symptoms in Indiana, where the ragweed pollen count is higher.

## Summary

The incidence of major allergic disorders in 2 groups of Negro children in Washington, D. C. has been reported.

One group comprised 1,565 individuals ranging in age from infancy to 15 years. Observations were made by pediatricians engaged in general private practice. The incidence of major allergic syndromes in this group was 10.5 per cent, with the following distribution: asthma 4.7 per cent, eczema 3.0 per cent, and allergic rhinitis 2.2 per cent.

The second group consisted of 666 school children ranging in age from 6 to 14 years. The study which was conducted by use of questionnaires revealed an incidence of major allergic syndromes of 16.6 per cent with the following distribution: asthma 6.3 per cent, eczema 2.5 per cent, and allergic rhinitis 4.5 per cent.

Although caution must be observed in comparing results reported by different investigators whose methods and places of study vary, certain similarities and differences are obvious. The general incidence in the Negro children is similar to that reported by some authors and lower than that reported by other authors whose subjects were predominately Caucasian. The comparative incidence for asthma and eczema is similar for the 2 races. The chief racial difference appears to be a lower incidence of allergic rhinitis in the Negro children, but this observation warrants further study.

The participating physicians who provided observations on the children in group 1 of this study were Drs. Clifford R. Booker, Pinyon L. Cornish, Robert P. Crawford, and Julian C. Perry.

The authors also wish to acknowledge the assistance of Dr. I. Blanche Bourne, Chief, School Health Services Division, Bureau of Maternal and Child Health, D. C. Department of Public Health, for providing access to the parents of the school children in group 2 of this study.

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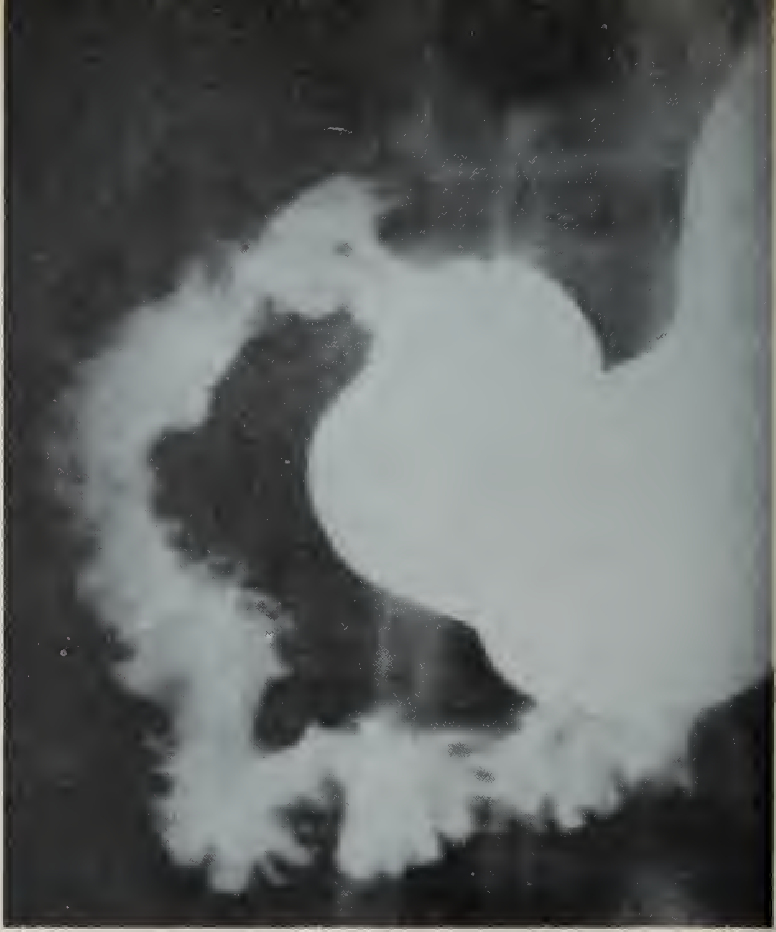

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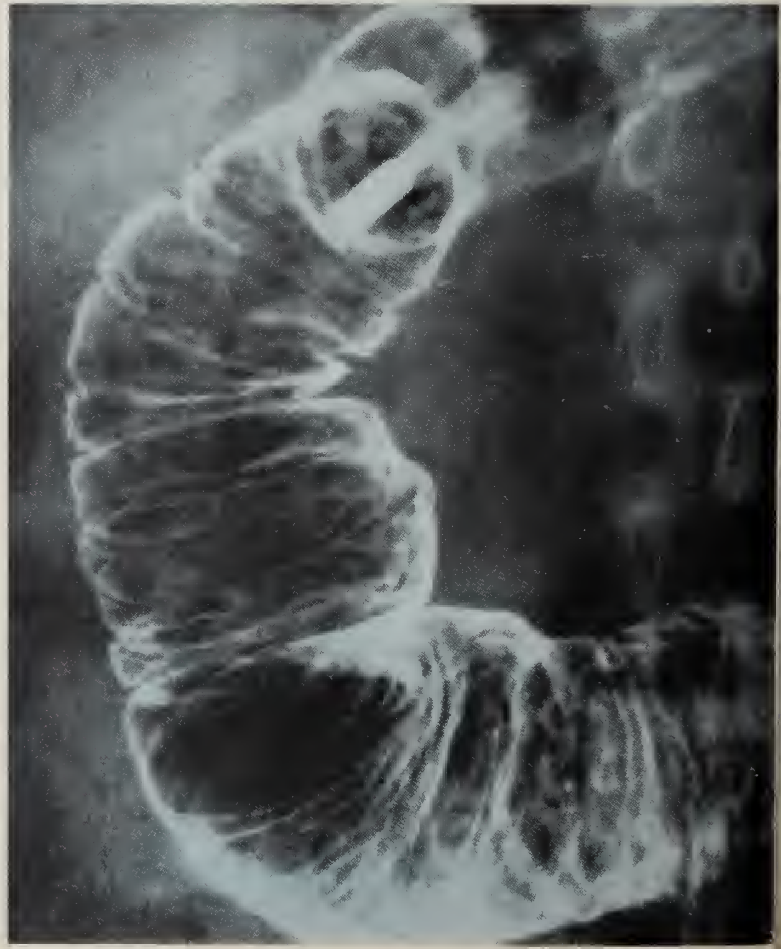

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Preludin is indicated only as an anorectic agent in the treatment of obesity. It may be used in simple obesity and in obesity complicated by diabetes, moderate hypertension, or pregnancy. For use in pregnancy, see Warning.

*Dosage:* One 25 mg. tablet b.i.d. or t.i.d. Or one 75 mg. Endurets® prolonged-action tablet a day, taken by midmorning. *Contraindications:* Severe coronary artery disease, hyperthyroidism, severe hypertension, nervous instability, and agitated prepsychotic states. Do not use with other CNS stimulants, including MAO inhibitors.

*Warning:* Do not use during first trimester of pregnancy unless potential benefits outweigh possible risks. There have been clinical reports of congenital malformation, but causal relationship has not been proved. Animal teratogenic studies have been inconclusive. *Precautions:* Use with caution in moderate hypertension and cardiac decompensation. Cases involving abuse of or dependence on phenmetrazine hydrochloride have been reported. In general, these cases were characterized by excessive consumption of the drug for its central stimulant effect, and have resulted in a psychotic illness manifested by restlessness, mood or behavior changes, hallucinations, or delusions. Do not exceed recommended dosage. *Side Effects:* Dryness or unpleasant taste in the mouth, urticaria, overstimulation, insomnia, urinary frequency or nocturia, dizziness, nausea, or headache. (B)R46-560-A

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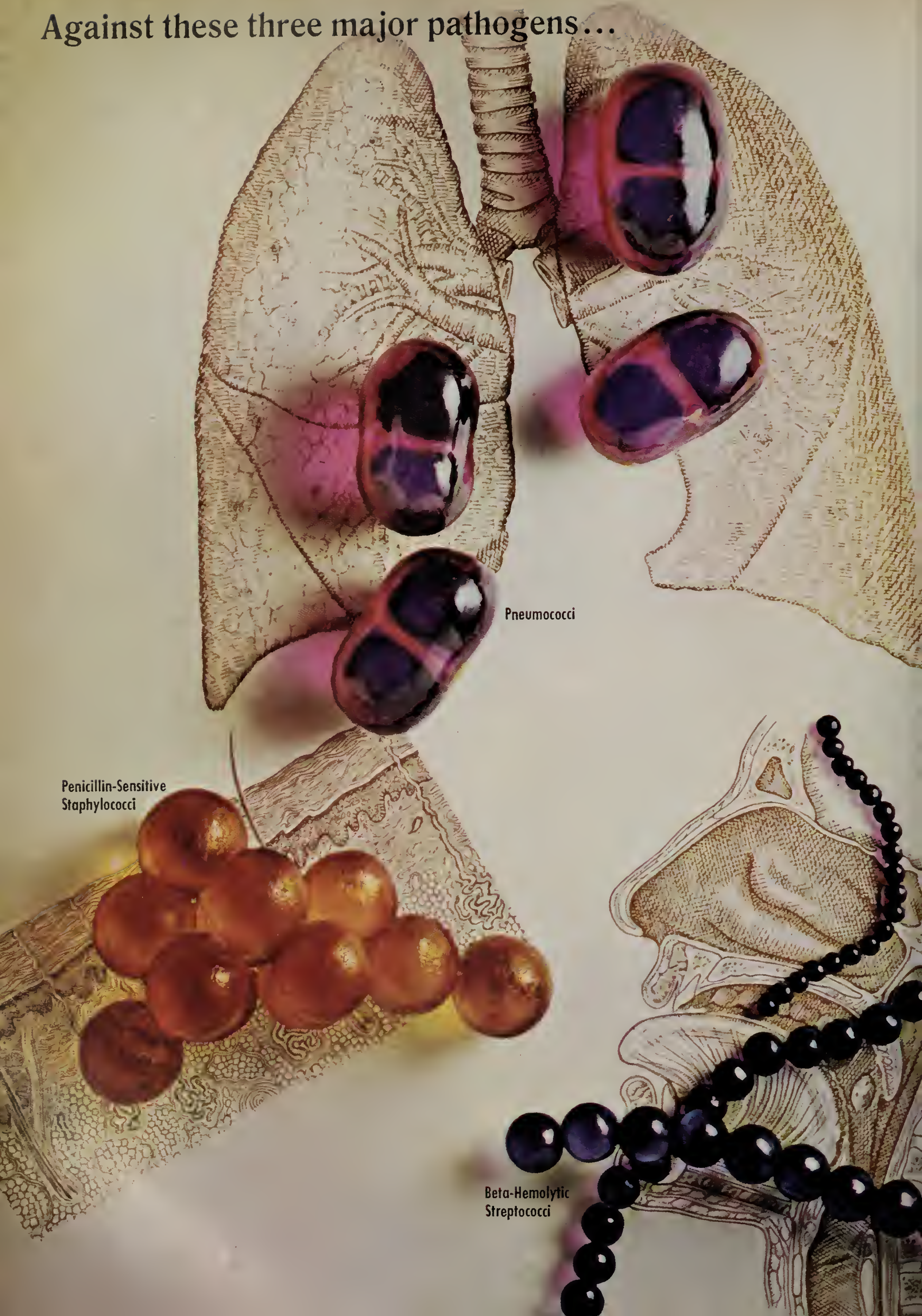
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Penicillin-Sensitive Staphylococci
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V-Cillin K® provides dependable oral antibacterial therapy

**because it combines a high degree of activity...**

V-Cillin K has been shown to be effective in the treatment of streptococcus and pneumococcus infections as well as infections caused by sensitive strains of staphylococci. It may be used for the prophylaxis of streptococcus infections in patients with a history of rheumatic fever and for the prevention of bacterial endocarditis after tonsillectomy in patients with a history of rheumatic fever or congenital heart disease.

**with high blood levels, even when taken with food**

V-Cillin K is stable in acid and immediately soluble. High serum levels, therefore, are reached rapidly. Because it is acid stable, V-Cillin K is well absorbed even when taken close to mealtime. These desirable properties help make V-Cillin K a dependable penicillin for oral use.

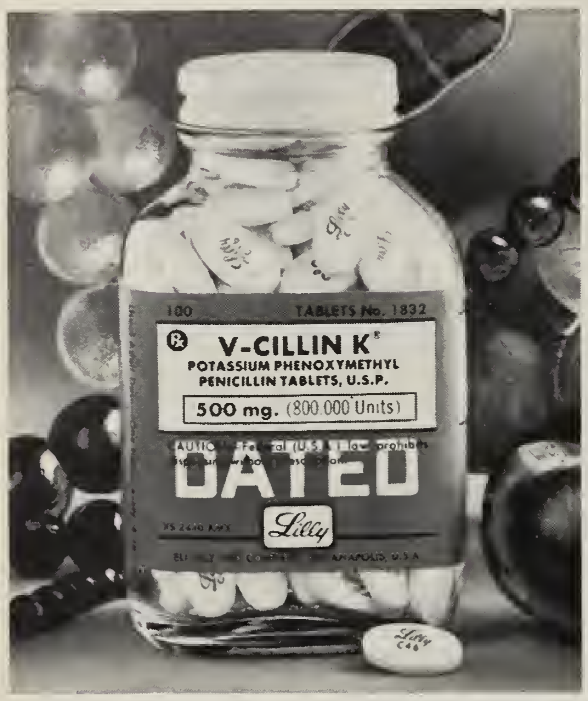
**V-Cillin K®** Lilly 701449

**Potassium Phenoxymethyl Penicillin**

**Now available: V-Cillin K®, Pediatric,
for Oral Solution, 250 mg. (400,000 units)
per 5 cc. of solution.**

*(See next page for prescribing information.)*

# New 500 mg. tablets...a more convenient way to give high doses



**Description:** V-Cillin K, the potassium salt of V-Cillin® (phenoxymethyl penicillin, Lilly), combines acid stability with immediate solubility and rapid absorption. Higher, more rapid serum levels are obtained than with equal oral doses of penicillin G.

**Indications:** Streptococcus, pneumococcus, and gonococcus infections; infections caused by sensitive strains of staphylococci; prophylaxis of streptococcus infections in patients with a history of rheumatic fever; and prevention of bacterial endocarditis after tonsillectomy and tooth extraction in patients with a history of rheumatic fever or congenital heart disease.

**Contraindication:** Penicillin hypersensitivity.

**Warnings:** In rare instances, penicillin may cause acute anaphylaxis which may prove fatal unless promptly controlled. This type of reaction appears more frequently in patients with a history of sensitivity reactions to penicillin or with bronchial asthma or other allergies. Resuscitative drugs should be readily available. These include epinephrine and pressor drugs (as well as oxygen for inhalation) for immediate allergic manifestations and antihistamines and corticosteroids for delayed effects.

**Precautions:** Use cautiously, if at all, in a patient with a strongly positive history of allergy.

In prolonged therapy with penicillin, and particularly with high parenteral dosage schedules, frequent evaluation of the renal and hematopoietic systems is recommended.

In suspected staphylococcus infections, proper laboratory studies (including sensitivity tests) should be performed.

The use of penicillin may be associated with the overgrowth of penicillin-insensitive organisms. In such cases, discontinue administration and take appropriate measures.

**Adverse Reactions:** Although serious allergic reactions are much less common with oral penicillin than with intramuscular forms, manifestations of penicillin allergy may occur.

Penicillin is a substance of low toxicity, but it possesses a significant index of sensitization. The following hypersensitivity reactions have been reported: skin rashes ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; and reactions resembling serum sickness, including chills, fever, edema, arthralgia, and prostration. Severe and often fatal anaphylaxis has occurred (see Warnings). Hemolytic anemia, leukopenia, thrombocytopenia, and nephropathy are rarely observed side-effects and are usually associated with high parenteral dosage.

**Administration and Dosage:** Usual dosage range, 125 mg. (200,000 units) three times a day to 500 mg. (800,000 units) every four hours. For infants, 50 mg. per Kg. per day divided into three doses.

See package literature for detailed dosage instructions for prophylaxis of streptococcus infections, surgery, gonorrhea, and severe infections.

**How Supplied:** Tablets V-Cillin K, U.S.P., 125 mg. (200,000 units), 250 mg. (400,000 units), and 500 mg. (800,000 units).

V-Cillin K, Pediatric, for Oral Solution, 125 mg. (200,000 units) and 250 mg. (400,000 units) per 5 cc. of solution (approximately one teaspoonful). [042567]

*Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana 46206.*

Lilly

701449

# PRESIDENT'S PAGE

## "CUSTOMARY AND REASONABLE..."

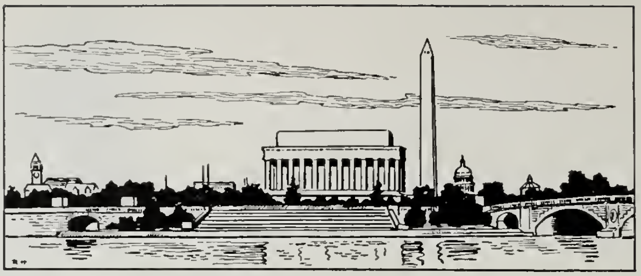
During the past 2 years the medical profession has been repetitively bombarded with the words "usual and customary," "reasonable," and "prevailing" with regard to payments allowed as benefits for subscribers to insurance plans, particularly those developed under Federal Government legislation. In many instances these terms define payments made directly to physicians, as exemplified by the assignment mechanism of Medicare, to which a large segment of the profession is vigorously opposed. How many of us really understand the meaning of these terms? An attempt to explain the significance of this language might be helpful.

The law states that "reasonable charges" are "the customary charges for similar services generally made by the physician . . ." and "the prevailing charges in the locality for similar service." "Customary charge" refers to the "uniform amount which the individual physician . . . charges in the majority of cases for a specific procedure or service." The reasonable charge cannot be higher than the customary charge. Furthermore, under Medicare the reasonable charge cannot exceed the charge applicable for a comparable service under comparable circumstances to the carrier's own policyholders. This limitation is perhaps the origin of much of the confusion and misunderstanding associated with payment practices. The carrier is the fiscal agent, in our case Blue Shield (Medical Service of D.C.), selected locally. Hence, the maximum ceiling on a given fee is determined by the benefit for such service. Medical Service elected to utilize as the guide in this regard its supplemental benefits plan, which represents its maximum fee allowance across the board, in order to provide the most equitable return to the physician and patient for professional services. Analysis of claims indicates that only a small number have exceeded this "ceiling."

"Prevailing charges" refers to those charges which fall within the range of charges most frequently and most widely used in a locality for particular services or procedures. Charges higher than "customary" or "prevailing" may be found to be "reasonable" under special circumstances and appropriate adjustment obtained by suitable documentation. This means that the law allows some flexibility so that payment for physicians' services can be expanded (1) when more than usual time, effort or skill is involved, (2) when changes occur applicable to the whole locality serviced by a given carrier, or (3) when specialty services of an unusual nature are provided under certain circumstances. However, it is clearly stated that the "income (of the beneficiary) is not to be taken into account by the carrier." "Robin Hood medicine" is thereby eliminated from the picture.

What all this adds up to, as I interpret it, is that "customary and prevailing" fee payments to physicians providing services to these beneficiaries, if the assignment mechanism is not invoked and if the patient pays his share of the co-insurance, would result in "full" recompense to the doctor for services rendered. The service must be adequately identified, special or unusual circumstances outlined, and a fair fee applied. If these criteria are met, the encroachment, economically at least, of third-party intrusion into the practice of medicine can be minimized.

Henry D. Ecker



# EDITORIALS

## A Thank You Note

I WAS BOTH FLATTERED and pleased that the issue of the ANNALS for September 1967 was planned by friends to commemorate my 35 years of continuous service as its Editor. You can imagine my surprise to discover that it was also to be a *festschrift* commemorating my years as a teacher at Georgetown prepared by my former Fellows (Assistants). This I appreciate more than words can express. One of my greatest satisfactions was working with these men and watching them "go up the ladder" to become physicians of outstanding ability. Another satisfaction was meeting ex-students wherever I went over the U. S. A., who greeted me cordially in spite of my reputation of being a "tough" professor. I have never met a Georgetown medical graduate who was not respected in his community.

I was the first full-time member of the clinical faculty at Georgetown (1929). Reorganization of the clinical teaching curriculum was indicated, and such distinguished clinical professors as George Tully Vaughan (surgery) and Prentiss Willson (obstetrics and gynecology) collaborated in bringing this about. Our objective was to make Georgetown a good medical school for educating bright young men (there were no women medical students at that time) to be good clinicians. Our clinical faculty at that time could not possibly engage in the type of postgraduate educational activities that Dean Rose described in his paper, "A System of Continuing Medical Education." I hope we contributed something to start the "ball rolling" toward our present advanced methods of medical education.

My service as Editor of the MEDICAL ANNALS OF THE DISTRICT OF COLUMBIA has been a pleasant although arduous one. For years I had to scrounge for medical papers and had to write quite a number for it myself. I had the help (and sympathy) first of Coursen B. Conklin, Secretary of the Society and Managing Editor, and then for many years of Theodore Wiprud, who succeeded Dr. Conklin. For quite a number of years now Miss A. Louise Eckburg, as full-time Assistant Editor, has been my good right arm. I appreciate all the coöperation I have had from members of the Society and local medical institutions in helping to make the ANNALS what it is. I have edited every article published in it for 35 years and have learned a lot by doing so.

Regarding the 2 books to which my name is attached, much credit goes to Dr. Wilfred M. Barton (Professor of the Theory and Practice of Medicine when I was a medical student) for the design of "Symptom Diagnosis" and to Dr. Hugh H. Hussey, who by copious and accurate notes of my lectures made it relatively easy for me to write "The Fundamentals of Internal Medicine." My thanks go to Dr. William M. Oliver, now of Santa Barbara, California, one of my former Assistants, for helping to revise both books, which, as all authors know, is more arduous than writing the original book.

Again, my thanks to all, and especially to Dr. Stephen W. Nealon and his committee, for preparing the September issue of the ANNALS in my honor.

WALLACE M. YATER

## Classification of Genetic Diabetes

THE COMMITTEE on Professional Education of the American Diabetes Association has published a classification of genetic diabetes mellitus as a special report in the July 1967 issue of *Diabetes*. This classification will be an aid to communication among physicians treating diabetes, between them and their patients, among those doing clinical research, and to those teaching the subject.

A classification of genetic diabetes mellitus based on abnormalities of carbohydrate metabolism is given below. Progression or regression from one stage to the next may never occur, may proceed slowly over many years, or may be very rapid. This classification does not consider the presence or absence of vascular disease, for patients with minimal glucose intolerance or even normal tolerance may have angiopathy.

1. *Overt diabetes mellitus.* This is frank diabetes, either of the ketosis-prone or ketosis-resistant type. Fasting hyperglycemia is present. Symptoms of hyperglycemia and glucosuria may be present. A glucose tolerance test is not required for diagnosis.

2. *Chemical or latent diabetes.* This is asymptomatic diabetes. The fasting blood glucose level may be elevated but is usually normal, and the postprandial level is frequently elevated. Oral or intravenous glucose tolerance tests performed in the absence of "stress" give results in the ranges accepted for diabetes.

3. *Suspected diabetes mellitus* (including "stress" hyperglycemia). Persons who have temporary carbohydrate intolerance in certain physiologic or pathologic situations should be suspected of having diabetes mellitus, particularly when there is a family history of diabetes. Symptoms due to severe hyperglycemia occurring during periods of "stress" should be regarded as representing overt diabetes until proved otherwise. Asymptomatic or symptomatic derangement of carbohydrate tolerance should be reëvaluated after total recovery from the "stress." In particular, impaired carbohydrate tolerance in the following situations requires long-term evaluation:

a. Pregnancy. The term "gestational diabetes" indicates the presence of abnormal glucose tolerance which reverts to normal following delivery. In these individuals follow-up studies have revealed a high risk of development of diabetes. (Diabetes should also be suspected in a woman whose obstetrical history includes large babies, unexplained abortions, fetal deaths, neonatal deaths, or hydramnios.)

b. Obesity with abnormal glucose tolerance which returns promptly to normal with moderate weight loss.

c. Infections, trauma, vascular accidents, burns, impaired nutrition, and severe emotional disturbances.

d. Treatment with pharmacologic agents, such as corticosteroids or thiazides.

e. Endocrinopathies such as acromegaly, Cushing's syndrome, thyrotoxicosis, and pheochromocytoma. (Diabetes must also be suspected in elderly subjects without symptoms and signs of the disease but with a glucose tolerance test which in younger individuals would be considered abnormal.)

4. *Prediabetes.* Prediabetes is a term applied to the period of time prior to the onset of identifiable diabetes mellius (overt, chemical, or latent). This is a conceptual term identifying the interval between fertilization of the ovum and the demonstration of impaired glucose tolerance in an individual predisposed to diabetes on genetic grounds but presently exhibiting a normal glucose tolerance. It cannot be diagnosed with certainty in the current state of our knowledge except in the nondiabetic identical twin of a diabetic patient and possibly in the offspring of 2 diabetic parents.

## A Presidential Invitation

Dear Doctor:

It is with great pleasure that I invite you to my home State this fall to attend the AMA Clinical Convention at Houston, November 26–29.

I believe you will find the Convention's program particularly interesting; it offers refreshing insights into clinical problems that you will find useful in your practice or professional duties.

This meeting is especially designed to help us keep up-to-date on latest medical developments. For the twenty-first consecutive year the AMA has assembled an extensive, well-rounded program outlining current knowledge.

You will be impressed, I think, by the outstanding medical teachers who have accepted the invitation of the Harris County Medical Society and the AMA Council on Scientific Assembly to participate in the scientific program. The Harris County Society has done a fine job in bringing together this program.

For you, the Clinical Convention presents opportunities for refreshing your medical knowledge, for renewing associations with fellow physicians, and for catching a breather from your busy schedule. It promises to be a stimulating 4 days, worthy of your time.

With my colleagues, the physicians of Texas and Harris County, I cordially invite you to Houston—a dynamic, interesting city that you and your family will enjoy.

See you at the Clinical!

Milford O. Rouse, M.D.
*President, American Medical Association*

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Dosage: Adults—1 tablet, swallowed whole to preserve timed-release feature, in morning, midafternoon and at bedtime. Side effects: Occasional drowsiness, blurred vision, cardiac palpitations, flushing, dizziness, nervousness or gastrointestinal upsets. Precautions: The patient should be advised not to drive a car or operate dangerous machinery if drowsiness occurs. Use with caution in patients with hypertension, heart disease, diabetes or thyrotoxicosis.

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# Question of the Month—?

**Should a physician charge a fee for services rendered over the telephone?**

### Answers and Comments

John W. Walsh, M.D. (Obstetrics-Gynecology): Basically NO.

In the practice of obstetrics and gynecology I constantly render services over the telephone. In many instances telephone consultation with patients in my care lightens my office load and I can care for many of their needs through this medium.

We are also often called by patients of colleagues from out of town. I believe that our profession demands that we extend the courtesy of telephone consultation to these people. I always feel that I can tell my patients to call on my colleagues in turn when they are in other cities.

There remains, however, a small group of patients who see their doctors perhaps once or so every several years and in the interim plague him with telephone calls. In these instances I don't believe that anyone would doubt the justification if a fee were charged.

John F. J. Clark, M.D. (Obstetrics-Gynecology): Whether a physician should charge a fee for services rendered over the telephone depends upon the type of practice and specialty in which he is engaged.

I do not believe that an obstetrician and gynecologist should charge for services rendered over the telephone. This should be part of the service that a patient can expect from him, and it helps to develop a good physician-patient relationship.

A patient likes to feel that she can contact her obstetrician at any time and ask any question that is of concern to her.

In the area of gynecology, postoperative patients should feel free to communicate with the physician without worrying about whether or not there is an additional charge for information given over the telephone.

William W. Funderburk, M.D. (Surgery): The physician in giving a telephone consultation has to answer the question sincerely whether he is truly giving the best advice possible under the circumstances or whether he is shirking his responsibility to the patient because of the added time involved in a visit with the patient. My personal feeling about advice given via the telephone is that it should represent an interim in the continuity of care for a situation in which the physician is already knowledgeable. For example: (1) Initial care is guided by phone only when there is competent personnel in attendance and I am going to see the patient sometime in the near future. (2) A change of medication is advised to a physician, nurse or patient when I have prior knowledge of the case.

Because of differences in interpretation of the same procedure by different individuals I prefer to reserve major decisions regarding patient care to those situations that I observe personally.

Since I prefer to view the telephone as a greater convenience to me under the above circumstances I do not believe that the patient should be charged for my consultations.

W. LeRoy Dunn, M.D. (Internal Medicine): A fee for service rendered by telephone can be readily justified. The time available to a physician determines what services he can render to a limited number of patients. It matters not what the physician's training, his skill, his ability, or his motivation, the number of patients he treats cannot exceed the time available for this.

While such charges can be justified, is it wise to make them? Many patients, most in fact, are not accustomed to being charged for services rendered over the telephone. Many will not understand it; others will probably resent it. From the standpoint of patient relations it may prove unwise.

If a physician makes such charges he should be sure that his patients understand the reasons for this policy and how it will be applied.

Orville W. Donnelly, M.D. (Internal Medicine): On the whole, I think not. I am reluctant to place a financial restraint on the single most important open line of communication between the patient and his physician. The policy of a fee for every service rendered, while fiscally sound, in this case may impede rather than contribute to good medical care.

Raymond Scalettar, M.D. (Internal Medicine): I do not believe physicians should charge a fee for services rendered over the telephone with the following exceptions:

I believe the time required to take care of the administrative processes of phoning in orders and discussing a patient to be admitted to the hospital is frequently inordinate. I believe this time factor should be considered in determination of the physician's fee.

In situations in which the patient abuses the telephone and becomes a nuisance with unnecessary and frequent phone calls, an appropriate fee is warranted. In particular, the phone call in the middle of the night by a patient with a trivial problem which could easily have waited until office hours should justify a fee for the abuse of telephonic communication.

Allan Coleman, M.D. (Pediatrics): There are 2 sides to this question: Telephone service establishes a doctor-patient relationship for which the physician is as responsible as for home-office or hospital service; therefore a charge might be justified because of the responsibility taken. However, such charges are poor public-relations makers, hard to collect, and rarely imposed in this locality.

The alternative, which is my personal choice, is to limit telephone services to minor advice and progress reporting and to insist on personal attendance otherwise. Telephone medicine tends to be poor medicine, in my experience. It is often worth only the usual local charge—zero.

Harold M. Hobart, M.D. (Pediatrics): No.

**If any members have dissenting views, your Editorial Staff will be pleased to receive and publish them.**

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SIDE EFFECTS of significance have not been reported. However, the risk of vaccine-induced poliomyelitis, estimated to be from 1:2,500,000 to 1:50,000,000 should be considered.

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# A Guide for Collaboration of Physician, Social Worker, and Lawyer in Helping the Unmarried Mother and Her Child*†

THE NEED for close coöperation between the physician, the social worker, and the lawyer in the care of the unmarried mother should be universally recognized. Each of these 3 is responsible for advising the unmarried mother of the need for consultation in her case with the other 2 disciplines involved because each has a special field of competence.

The physician is held responsible for the physical and mental health of the patient. It is the physician who must make the diagnosis of pregnancy, determine the expected date of delivery, and decide where the delivery should take place. Among other things he must decide how much information the patient should be given on the physiology and pathology of pregnancy, labor, and the puerperium. His decision on whether to advise the patient to nurse the baby (if she decides to keep him) will rest on emotional as well as physical factors.

He must safeguard the confidentiality of the information the patient discloses except as provided by the laws of his state. Recognizing the limitations placed on a minor, he must be certain of the validity of the consent the patient gives for any disclosures, treatment, or procedure. If social services are available the physician should avoid becoming involved with the placement of the infant or acting as an intermediary.

The responsibility of the social worker includes helping the unmarried mother with the distinctive social and emotional problems connected with having a child out of wedlock. To this end, the social worker draws upon the experience of social agencies in working with unmarried mothers, upon familiarity with community resources, and upon social and psychological diagnostic skills in determining what help a particular client needs and can use. Among other things this involves referring the patient for early and competent obstetrical examination, emphasizing the need for continued antepartum and postpartum care, reinforcing the medical care by strengthening the faith of the patient in the doctor, and, where possible or necessary, implementing his recommendations.

The social worker counsels the patient on plans for her future and that of the infant, always safeguarding the best interests of the child. The social worker provides psychological help and support complementing that given by the doctor. The social worker recognizes and supports the legal obligations of the doctor as to the results of treatment or advice, including professional disclosures and the peculiar problems of a minor.

The social worker counsels the unmarried mother in the various social aspects involved and recommends that she consult a lawyer for advice on the legal aspects as needed in the individual situation.

The lawyer for the unmarried mother is responsible for counseling her regarding the legal consequences of keeping or of giving up her child and of her legal rights in respect to the putative father. If she releases the child for adoption, the lawyer must be sure that all legal requirements are met. He should not represent the prospective adoptive parents. If social services are available the lawyer should avoid becoming involved with the placement of the infant or acting as an intermediary.

All 3 disciplines recognize the right of the unmarried mother to make decisions for herself and her child except where such rights are involuntarily terminated by court action. Likewise, all 3 recognize that each must give advice and guidance to her. Whether giving advice is limited to mere clarification of the alternatives between which the client must choose or extends to a firm recommendation for the course of action the patient should take, the collective counseling like parental guidance, must be harmonious lest the unmarried mother become confused. Differences of opinion which may arise as to the advice to be given should be resolved by prior conferences.

Broad principles have been established through experience in all 3 professions, but philosophies vary in different communities and change from time to time not only within the same community but also within the Nation.

Furthermore, each case must be individualized, particularly with reference to questions such as:

1. Shall the parent of the patient or the putative father be told of the pregnancy?
2. Shall the patient marry the putative father?
3. Shall legal action be taken against him?
4. Where shall delivery take place?
5. Shall the putative father visit the patient before or after delivery?
6. Shall he ever see the baby?

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* The Guide has been approved by the Executive Board of The American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, the American Medical Association, the Family Law Section of the American Bar Association, the Child Welfare League of America, and the U.S. Children's Bureau.

† Reprinted from ACOG Technical Bulletin, No. 7, May 1967.

## Barbiturates as Suicidal Poisons

Barbiturates and the related minor tranquilizers are high on the list of suicidal poisons. Extreme care must be used in writing prescriptions for tranquilizers for patients, particularly those who are anxious or depressed. The physician should not write prescriptions for lethal quantities of these drugs, and they should not ordinarily permit renewal of the prescription without evaluating the patient.

Committee on Problems
of Drug Dependence
*Washington Psychiatric Society*

N.B. The Committee would appreciate it if members of the D. C. Medical Society will comment on or relate their experiences concerning problems of drug abuse or misuse.

7. Shall the baby be photographed and the picture made available?

8. Shall the patient be allowed, urged, or forbidden to see her child, put him to breast, or care for him?

9. Shall the patient have psychiatric help; if so to whom shall she be referred?

10. At which point in the pregnancy or puerperium shall the decision be made as to the child's future?

11. If the decision is for adoption, how and where shall final surrender of the child be taken?

12. Shall the mother be told of any deformity or handicap of the child, and if so, when and by whom?

13. If the matter of legal residence is involved and the possibility of non-adoptability, who shall be responsible for properly informing and counseling the unmarried mother?

When the doctor, social worker, and lawyer are mature, experienced individuals, each primarily concerned with working out the complex problems in any given case for the best interests of the child and the unmarried mother, each recognizing and respecting the responsibilities and competence of the other derived from professional training in dealing with the physical, mental, emotional, social and legal factors involved, there rarely will be a difference of opinion. If such a difference does arise, one which cannot be resolved by a conference, genuine collaboration requires the wholehearted assistance of all 3 in supporting the judgment of the member of the discipline with primary responsibility, namely: for the physical and mental health of the mother and child, the doctor; for the social and emotional welfare of the mother and child, the social worker; and for the legal protection of the mother and child, the lawyer.

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# DOCPAC Briefs

### or
### For the Record

The Board of Directors of DOCPAC (District of Columbia Political Action Committee) hopes that all members of the Medical Society are interested in the activities of DOCPAC during the past few months. After all, every organization, group, and committee has a purpose and a function.

In this report we should like to fill you in completely. DOCPAC has sent funds to AMPAC (American Medical Political Action Committee) which have been distributed to some 180 House and Senate races throughout the country. Further funds have been sent which will be placed in key Congressional and Senate races in the coming elections in November 1968. Some of these funds will also be used for crucial primaries. Therefore, DOCPAC funds have truthfully gone into every state of the Union and into one-third to one-half of all Congressional races. The money is used mostly in marginal races.

Second, your DOCPAC Board of Directors has sent money directly to a Democrat and a Republican member of the House of Representatives' District Committee.

Third, DOCPAC funds have gone to a Republican and a Democrat member of the Ways and Means Committee of the House. Both are vitally interested in good medicine.

Fourth, DOCPAC has gone on record in support of 3 nominees submitted to President Johnson for appointment to the new District of Columbia Council under the reorganization plan. None of the 3 nominees, who are members of DOCPAC, was named by the President.

If you are an interested citizen, which we believe every physician is, and have not yet joined DOCPAC, please do. The dues are: $20 for an individual per year, $30 for family membership, and contributions up to $99.99 accepted. If you have not joined, join now and send your money to: DOCPAC, 825 New Hampshire Avenue, N.W., Washington, D. C. 20037.

William H. Cooper, M.D.
*Chairman, D. C. Political*
*Action Committee*

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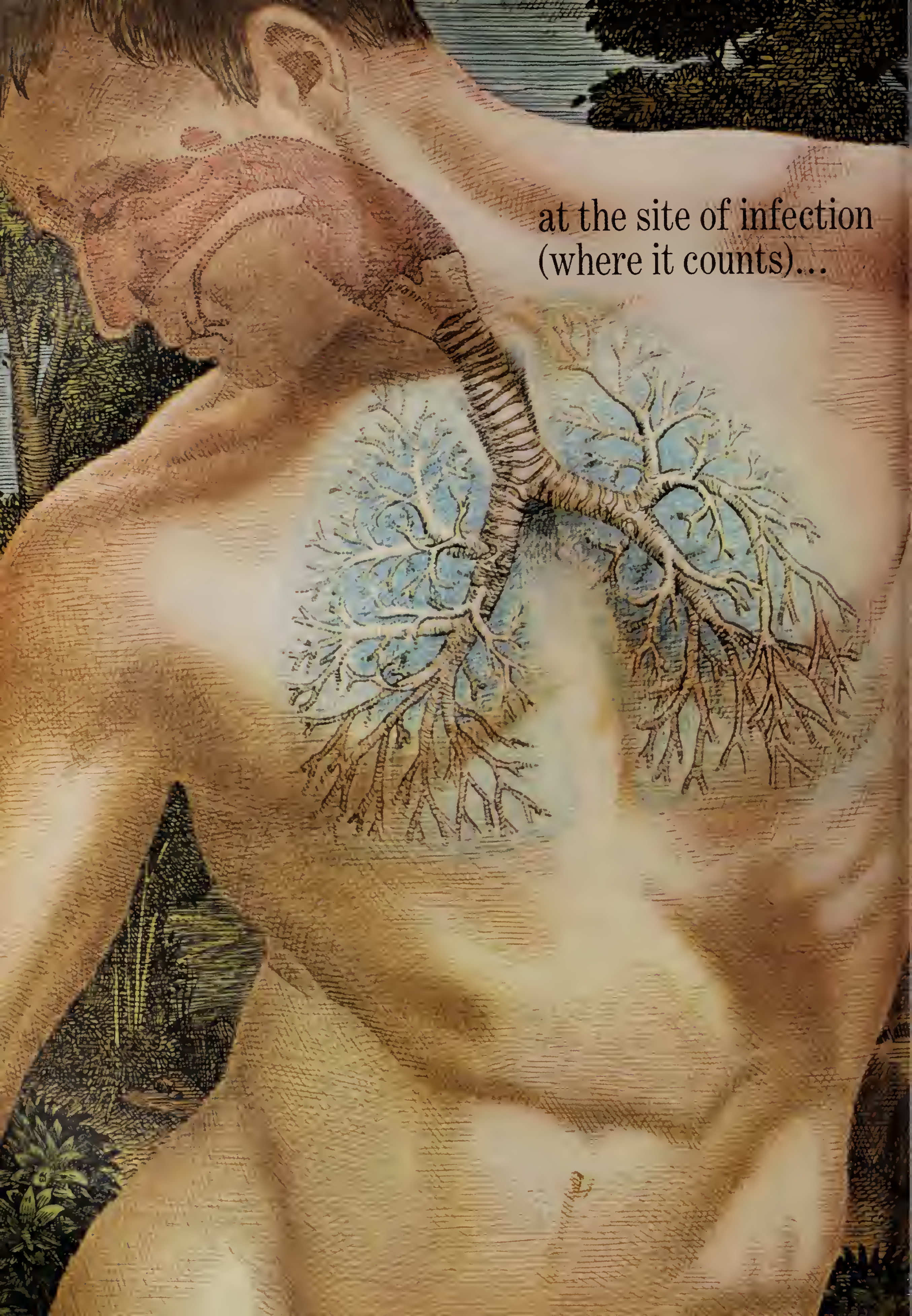
THE NATIONAL DRUG COMPANY
DIVISION OF RICHARDSON MERRELL INC
PHILADELPHIA, PENNSYLVANIA 19144

**Prescribing Information: Composition:** Each white, beveled, compressed tablet contains: Quinine Sulfate 260 mg. and Aminophylline 195 mg. **Contraindication:** QUINAMM is contraindicated in pregnancy because of its quinine content. **Precautions:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. Discontinue use if ringing in the ears, deafness, skin rash, or visual disturbances occur. **Dosage:** One tablet upon retiring. Where necessary, dosage may be increased to one tablet following the evening meal and one tablet upon retiring. **Supplied:** Bottles of 100 and 500 tablets. **References:** 1. Shuman, C.: Am. J. Med. Sci., 225:54, 1953. 2. Perchuk, E., et al.: Angiology, 12:102, 1961. 3. Rawls, W., et al.: Med. Times, 87:818, 1959. 6/67 Q-706A


at the site of infection
(where it counts)...

# Ilosone® provides more antibacterial activity than any other oral erythromycin

**Acid stable, better absorbed . . . Ilosone produces faster, higher, more prolonged blood levels, even in the presence of food[1-3]**

Because it is the most active form of oral erythromycin, Ilosone can help assure consistently greater antibacterial activity at the site of infection. Ilosone produces peak antibacterial blood levels two to four times those of other erythromycin preparations.[1,2] Not only are these levels attained earlier, but they are maintained for much longer periods. Even the presence of food does not seem to affect the activity of Ilosone.[1,3]

In the treatment of patients with bacterial infections susceptible to erythromycin, Ilosone has compiled an excellent therapeutic record. Since it exerts its greatest activity against gram-positive organisms, it is particularly useful in common respiratory and soft-tissue bacterial infections. Ilosone kills—not merely inhibits—streptococci, pneumococci, and more strains of staphylococci than any other macrolide antibiotic. This bactericidal action, coupled with the high antibacterial levels attained, makes Ilosone especially valuable in patients with low host resistance, such as infants, debilitated individuals, and diabetics.

Ilosone has shown no cross-resistance with penicillin and may be effective against organisms that have become resistant to that agent. Despite its high antibacterial activity, Ilosone has demonstrated a low incidence of side reactions. Blood dyscrasias, ototoxicity, and tooth staining have not been observed. Infrequent cases of drug idiosyncrasy, manifested by a cholestatic jaundice, have occurred, but there have been no known definite residual effects.

**Now available:**
New! Ready-mixed Ilosone Liquid 125! (Contains erythromycin estolate equivalent to 125 mg. erythromycin base per 5-cc. teaspoonful.)

701464

**Ilosone®**
**Erythromycin Estolate**

Lilly

*(See next page for prescribing information.)*

# Ilosone®/the most active oral form of erythromycin

**Description:** Ilosone is the most active form of oral erythromycin that has been developed. Because it is stable in acid, well absorbed, and excreted in lesser amounts in the bile, it provides faster, higher, and longer-lasting levels of antibacterial activity (ABA) in the serum, even when taken with food, than do comparable doses of erythromycin.

**Indications:** Ilosone is indicated in infections caused by micro-organisms sensitive to its action—especially staphylococci, hemolytic streptococci, and pneumococci.

It has been effective in streptococcus infections, particularly acute bacterial pharyngitis and tonsillitis; staphylococcus disease, including soft-tissue infections, furunculosis, abscesses, cellulitis, carbuncles, and wound infections; pneumococcus pneumonia and acute bronchitis with pneumococci on culture, bronchopneumonia, and otitis media.

In serious staphylococcus infections, erythromycin preparations should be used only in combination therapy with other antimicrobial agents; surgical procedures should be performed when indicated, and large doses of the antimicrobial agents should be employed.

Penicillin is the drug of choice for syphilis and gonorrhea, but Ilosone in multiple 500-mg. doses has been useful in patients with a history of penicillin allergy. Also, other infections due to susceptible bacteria in patients hypersensitive to penicillin or other antibiotics may be considered for treatment with Ilosone.

**Contraindications: Known history of sensitivity to this drug; preexisting liver disease or dysfunction.**

**Adverse Reactions:** Hepatic dysfunction with or without clinical jaundice has been reported infrequently. Changes in liver function tests indicative of intrahepatic cholestasis appear to be the result of individual idiosyncrasy. Findings subsided when treatment was discontinued. Occasionally, symptoms simulated extrahepatic obstructive jaundice or the colic of biliary tract disease.

When jaundice appeared to be related to use of the drug, laboratory findings were characterized by increased direct-reacting bilirubin, elevated alkaline phosphatase levels, negative or weakly positive cephalin flocculation and thymol turbidity tests, elevated serum glutamic oxalacetic transaminase levels, peripheral eosinophilia, and normal cholecystograms.

Gastro-intestinal disturbances not associated with hepatic effects and occasional allergic manifestations (urticaria, skin eruptions, and, rarely, anaphylaxis) have been reported. The normal intestinal gram-negative bacterial flora is not appreciably altered by erythromycin drugs.

**Administration and Dosage:** Ilosone is administered orally.

Infants and children under twenty-five pounds, 5 mg. per pound every six hours; twenty-five to fifty pounds, 125 mg. every six hours. Adults and children over fifty pounds, 250 mg. every six hours.

For severe infections, double the dosage. When larger doses are indicated, consider parenteral erythromycin therapy. In beta-hemolytic streptococcus infections, maintain treatment for ten days to prevent rheumatic fever or glomerulonephritis.

In syphilis, a total of 20 to 30 Gm. is administered in divided doses for ten to fifteen days. Close follow-up is necessary since erythromycin drugs have not had adequate evaluation in all stages of syphilis. Examination of spinal fluid is recommended during follow-up.

In gonorrhea, the dosage is 500 mg. four times a day for four days. Patients with a suspected lesion of syphilis should have a dark-field examination before receiving antibiotics and monthly serologic tests for three months. For detailed information, consult the package literature.

**How Supplied:** Pulvules® Ilosone, Capsules, N.F., 125 mg.* and 250 mg.*

Ilosone Liquid 125, Oral Suspension, U.S.P., 125 mg.* per 5-cc. teaspoonful.

Ilosone, 125, for Oral Suspension, N.F., 125 mg.* per 5-cc. teaspoonful.

Ilosone Drops, 5 mg.* per drop.

Tablets Ilosone Chewable, N.F., 125 mg.*

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*Base equivalent. [080967]

*References:* 1. Griffith, R. S., and Black, H. R.: Am. J. M. Sc., *247*:69, 1964. 2. Griffith, R. S., and Black, H. R.: Antibiotics & Chemother., *12*:398, 1962. 3. Hirsch, H. A., Pryles, C. V., and Finland, M.: Am. J. M. Sc., *239*:198, 1960.

*Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana 46206.*

Lilly

701464

# The Physician and the National Library of Medicine*

LEONARD KAREL, PH.D†

When the National Library of Medicine was established in 1836 as the Library of the Surgeon General's Office (U. S. Army), the Surgeon General was authorized to spend $150 for medical literature. Today the Library, located at Bethesda, Maryland, near Washington, in a 5-story contemporary building which it has occupied since 1962, is regarded as the world's largest in biomedicine. Among its holdings of 1,300,000 items, in 70 languages, are 315,000 monographs, 310,000 bound journal volumes, 285,000 theses, 168,000 pamphlets, and 4,500 reels of microfilm.

The Library provides 175,000 interlibrary loans annually, and of these 160,000 are photocopies of journal articles not available at the requesting local library. Reference personnel answer 10,000 personal inquiries, 10,000 phone inquiries, and 2,000 mail inquiries each year. Requests for 100,000 library items are made by 25,000 to 30,000 persons who use the reading room each year.

The Library is a major publisher of biomedical bibliographies, e.g., *Index Medicus, Cumulated Index Medicus, Bibliography of Medical Reviews, Biomedical Serials 1950-1960, Bibliography of the History of Medicine,* and *NLM Current Catalog.* Among other Library publications are *Medical Subject Headings,* the thesaurus for *Index Medicus; List of Journals Indexed in Index Medicus; National Library of Medicine Classification;* and *Russian Drug Index.*

## The National Library of Medicine

Known for 86 years as the Library of the Surgeon General's Office, the Library was developed as both a national and an international resource by Dr. John Shaw Billings, Librarian from 1865 to 1895. In 1922 it was renamed the Army Medical Library, and in 1952 it was again renamed, the Armed Forces Medical Library. In 1956, under legislation introduced by Senators Lister Hill of Alabama and John F. Kennedy of Massachusetts, it was transferred to the Public Health Service, Department of Health, Education, and Welfare, and named the National Library of Medicine.

The Library was established by the Congress of the United States to assist in the advancement of medical and medically related sciences by the collection, dissemination, and exchange of scientific and other information important to the progress of medicine and of public health.

Toward fulfillment of its mission the Library (1) acquires and preserves books, periodicals, films, prints, and other library materials pertinent to medicine; (2) organizes these materials by appropriate cataloging, indexing, and bibliographic listings; (3) publishes and disseminates catalogs, indexes, and bibliographies; (4) distributes materials through interlibrary loans, photographic, or other copying procedures; (5) provides reference and research assistance; and (6) encourages, promotes, and supports activities to further the progress of medicine and of public health by strengthening existing services and developing new ones.

The Congressional mandate was strengthened recently when, on October 22, 1965, President Johnson signed the Medical Library Assistance Act, Public Law 89-291 of the 89th Congress. In signing the Act the President commented that the Nation's medical libraries are a vital link between medical education, practice, and research, and that too little attention has been given to the problem of collecting and sharing scientific knowledge.

The Medical Library Assistance Act is an amendment to the legislation authorizing the establishment of the Library. The Act permits assistance to medical libraries for construction and renovation, for acquisition and for improvement of resources, for training of medical librarians and other information specialists, for preparation of publications, for research in medical library science, and for the development of regional medical libraries. The Act also authorizes traineeships, fellowships, and special scientific projects by individuals or institutions.

Administration of the Act on behalf of the Library is done by the Library's Extramural Programs.

The Library today serves as the principal national focus of resources and programs for better-ing communication in medicine and the health sciences and is encouraging the development of the existing system of medical libraries into a national medical information network. On July 1, 1967, the Library acquired the Public Health Service Audiovisual Facility in Atlanta, Georgia. This facility, renamed the National Medical Audiovisual Center, will coördinate a national program in biomedical audiovisuals.

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* Reprinted by permission from Pennsylvania Medicine, 1967, 70, 64.

† Special Assistant to the Associate Director for Intramural Programs, National Library of Medicine, 8600 Rockville Pike, Bethesda, Maryland 20014.

Access to the collection is facilitated through an interlibrary loan program. When libraries request loans through medical library channels, the National Library of Medicine lends books within the United States and, worldwide, provides single copies of articles from journals which the requesting libraries do not possess and which are not available locally. There is no charge for this service or for other services except special photography.

The Library collects materials comprehensively in some 40 biomedical subject categories and selectively in many related categories. The collection, in which are over 19,000 serial titles, is increased annually by 95,000-100,000 items. It is estimated that the Library now stores 360 million pages, of which 85 million are pre-1870, and that at least 10 million more are being acquired annually.

Its History of Medicine Division alone has between 60,000 and 65,000 printed works bearing publication dates earlier than 1801. Included in the collection are: an Arabic manuscript of the year 1094 on gastrointestinal disease; a collection of palm-leaf manuscripts from Ceylon, in Singhalese; works of Hippocrates and Galen; and letters written by George Washington, by Benjamin Rush, and by Florence Nightingale. Holdings also include 535 incunabula; 33,000 16th, 17th, and 18th century monographs; 1,600 17th century theses and pamphlets; 2,000 early American medical works; and an estimated 60,000 prints and photographs.

### Computerized Library Services

Efforts of conscientious, busy practitioners to achieve and to maintain awareness of the most recent medical discoveries and applications have often led to many and continuing frustrations. The increase in the volume of medical literature and in the number of users has not been paralleled by equivalent growth of medical libraries and of information storage and retrieval methods and facilities adequate to catalog, index, store, and retrieve literature for use of physicians, scientists, and others. Therefore, the Library adopted computerization as a means of assisting, supplementing, and complementing traditional approaches to management of published biomedical literature and pioneered in the use of computers for storage and retrieval of bibliographic information.

In January 1964 a computer-based information storage and retrieval system called MEDLARS (Medical Literature Analysis and Retrieval System) became operational at the Library.

MEDLARS joins the professional experience of trained literature analysts and searchers with the processing capabilities of a high-speed electronic computer. The literature analysts, using terms selected from a thesaurus of approximately 7,000 terms, *Medical Subject Headings* (Part II of the January issue of *Index Medicus*), characterize each article by assigning to it a number of subject headings or descriptors. Indexed articles are entered into the computer and transferred to magnetic tapes for storage, and for rapid retrieval. Currently, MEDLARS contains over 550,000 citations to biomedical journal articles published since January 1964. About 55 per cent of these are in English.

MEDLARS has improved the quality of the Library's monthly *Index Medicus* and has substantially reduced the time required for the production of other Library bibliographies.

*Index Medicus*, a comprehensive, monthly subject-author index, now incorporates 180,000 articles annually from nearly 2,300 of the world's biomedical journals. At the close of each calendar year MEDLARS compiles *Cumulated Index Medicus*, a complete listing, with cross-references, of the citations which were printed in that year's issues of *Index Medicus*. An abridged edition of *Index Medicus* for the personal use of physicians is being planned in coöperation with the American Medical Association.

(MEDLARS does not now include monographs, symposia, conferences, congresses, and proceedings not published in journals.)

The journals indexed in *Index Medicus* (approximately 2,300) are selected with the advice of an extramural committee whose decisions are made largely on the quality of the journal under consideration; however, care is taken to assure subject balance. Discussions of journals are based on prior knowledge of the journal and on inspection of the journal by committee representatives. In addition, the committee is assisted by advice from subject specialists. Comprising the present committee are physicians and scientists, medical editors, and medical librarians.

MEDLARS makes possible rapid machine searches of biomedical journal literature to obtain answers to reference questions that cannot be handled expeditiously by manual searches. Machine searches which provide citations to medical literature in specific areas of interest are called "demand bibliographies."

MEDLARS is responding to more than 400 highly specific computer search requests monthly. These requests are coming chiefly from physicians, teachers, and researchers in medical schools, hospitals, universities, and Federal research laboratories.

In addition to demand bibliographies, the Library collaborates with professional societies and other professional organizations in the preparation of "recurring bibliographies"—formally published, widely distributed bibliographies in specialized subject areas of broad interest.

These recurring bibliographies are *Artificial Kidney Bibliography*; *Bibliography of Medical Education*; *Cerebrovascular Bibliography*; *Fibrinolysis, Thrombolysis, and Blood Clotting*; *Index of Rheumatology*; *Index to Dental Literature*; and *International Nursing Index*.

Although the Library supplies the sponsoring organization with citations retrieved periodically from MEDLARS on film ready for offset printing, publishing and distributing the bibliography, on a nonprofit basis, are the responsibility of the sponsoring organization.

At frequent intervals, generally monthly, the Library selects from its demand bibliographies a few considered to be of general interest. Announcements of the availability of these bibliographies, called *NLM Literature Searches*, appear in *Journal of the American Medical Association*, *Public Health Reports*, *Journal of the American Dental Association*, *NLM News*, and other publications including state journals. There is no charge for these *Searches*. Clinicians, educators, and researchers interested in receiving notices on new *NLM Literature Searches* may write to the Office of Assistant to the Director, National Library of Medicine, 8600 Rockville Pike, Bethesda, Maryland 20014.

To enhance effectiveness of MEDLARS, the Library has provided its computer tapes and programs to university-affiliated centers which can make computer-generated demand bibliographies available locally or regionally to qualified practitioners, educators, and researchers. Decentralized MEDLARS stations are now in operation or will soon be in operation at Harvard University, the University of Alabama, the University of California at Los Angeles, the University of Colorado, and the University of Michigan. Others are being considered, and as regional libraries, authorized by the Medical Library Assistance Act, are identified, they too will be provided with a MEDLARS search capability.

Two MEDLARS centers are in operation outside the United States: In the United Kingdom under a coöperative arrangement between the University of Newcastle-upon-Tyne and the National Lending Library for Science and Technology at Boston Spa, Yorkshire, demand bibliographies are provided by the Lending Library. In Sweden, literature references taken from MEDLARS tapes are provided by the Karolinska Institutet in Stockholm.

Physicians wishing to obtain demand bibliographies are encouraged to seek the advice of local medical librarians on suitability of the inquiries and on the preparation of requests which will elicit the information sought. The use of *Medical Subject Headings, Guide to MEDLARS Services*, and an expression of specific interests will help avoid retrieval of irrelevant citations. Thus, a request specifying animal experiments will help to insure that citations on human studies will not appear in the bibliography; similarly, specifying a single age group will obviate retrieval on all age groups.

Citations may be arranged alphabetically by senior author, by journal title, by language, by subject headings, and by year of publication, and each citation can be printed with the descriptors assigned to it by its indexer. Although the computer can print bibliographies on 8½ by 11-inch paper or on 3 by 5-inch cards, usually the printout is provided on the less costly paper.

The elapsed time between receipt of a request and mailing of a bibliography is a function of the volume of searches requested. At present elapsed time is about 3 weeks.

It is important to note that MEDLARS does not produce abstracts. It is also important to note that MEDLARS services are not provided for searches which can be conveniently and readily accomplished by the use of published indexes, handbooks, and other reference materials.

### Demand Bibliography Requests from Washington, D. C.

During the period July 1966–June 1967, inclusive, the National Library of Medicine responded to 364 demand bibliography requests from biomedical personnel in Washington, D. C.

Subjects ranged from Myopathy and Hyperglobulinemia, and Electrocardiographic Wave Forms and Somatotypes, to Differential Diagnosis of Lung Neoplasms and Lymphomas.

The distribution of the 364 requests was:

| | |
|---|---|
| Catholic University | 9 |
| Gallaudet College | 2 |
| George Washington University | 13 |
| Georgetown University | 46 |
| Howard University | 2 |
| St. John's High School | 1 |
| Federal | 271 |
| Other | 20 |
| Total | 364 |

### Summary

The National Library of Medicine, now the world's largest biomedical library, was established by Congress to further the advancement of medical and medically related sciences by the collection, dissemination, and exchange of scientific and other information important to the progress of medicine and of public health. It has become an international as well as a national resource for publications and other items relevant to medical communication, and renders service on a worldwide basis.

In January 1964 a computer-oriented information storage and retrieval system called MEDLARS (Medical Literature Analysis and Retrieval System) became operational at the Library. This system has improved the quality of *Index Medicus* and other Library-associated publications and has substantially reduced the time required for preparation and publication of such publications.

The MEDLARS store of biomedical journal articles published since January 1964 now exceeds 550,000 and is growing at an annual rate of 180,000 articles, taken from nearly 2,300 journals. Requests for computer searches come chiefly from physicians, teachers, and scientists in medical schools, hospitals, universities, and Federal research laboratories.

During the period July 1966–June 1967, inclusive, the National Library of Medicine responded to 364 demand bibliography requests from biomedical personnel in Washington, D. C.

## New Members

### Active

Raymond Isaac Band, M.D. Office: 1800 R Street, N.W. Born in Chicago, Ill., he received his medical degree from George Washington University in 1948. Specialty: Psychiatry.

Martin Gerard Durkin, M.D. Office: Georgetown University Hospital. Born in Philadelphia, Pa., he received his medical degree from Jefferson Medical College in 1961. Specialty: Gastroenterology.

Alina Maria Efron, M.D. Office: 4607 Connecticut Avenue, N.W. Born in Poland, she received her medical degree from Warsaw University, Poland, in 1943. Specialty: Psychiatry.

Edmond James Fitzgerald, M.D. Office: 4307 Branch Avenue, Marlowe Heights, Md. Born in New York City, he received his medical degree from Georgetown University in 1959. Specialty: Urology.

Frederick Joseph Grigsby, M.D. Office: 3472 14th Street, N.W. Born in Dayton, Ohio, he received his medical degree from Meharry Medical College in 1947. Specialty: Urology.

Nicholas Edward Gwozdz, M.D. Office: 1714 N Street, N.W. Born in Springfield, Mass., he received his medical degree from Georgetown University in 1961. Specialty: Internal Medicine.

Donald David Haut, M.D. Office: Southwest Health Center. Born in Wilmington, Delaware, he received his medical degree from Temple University in 1958. Specialty: Internal Medicine.

Carol G. Jacob, M.D. Office: 309 N Street, S.W. Born in Hamburg, Germany, she received her medical degree from Woman's Medical College of Pennsylvania in 1961. Specialty: Psychiatry.

Robert Ephraim Jacobs, M.D. Office: DeWitt Army Hospital, Ft. Belvoir, Va. Born in Boston, Massachusetts, he received his medical degree from Tufts Medical School in 1961. Specialty: Radiology.

Tumkur Madhu, M.D. Office: Glenn Dale Hospital, Glenn Dale, Md. Born in Tumkur, India, he received his medical degree from the University of Mysore, India, in 1949. Specialty: Physical Medicine.

Essex Crystol Noel III, M.D. Office: 6601 14th Street, N.W. Born in Salem, Virginia, he received his medical degree from Meharry Medical College in 1948. Specialty: Psychiatry.

Carlos Alberto Silva, M.D. Office: 1712 Eye Street, N.W. Born in Mayaguez, Puerto Rico, he received his medical degree from George Washington University in 1960. Specialty: General Surgery.

### Associate

John Andrew Pottiglione, M.D. Office: 6343 Livingston Road, Oxon Hill, Md. Born in McIntyre, Pennsylvania, he received his medical degree from Seton Hall College of Medicine in 1962. Specialty: Pediatrics.

Milton Corn, M.D. Office: D. C. General Hospital. Born in Berlin, Germany, he received his medical degree from Yale University in 1955. Specialty: Hematology.

Gary D. London, M.D. Office: 1200 19th Street, N.W. Born in Sioux City, Iowa, he received his medical degree from New York University College of Medicine in 1961. Specialty: Obstetrics-Gynecology.

# Health Dept. Notes

## Services for the Aged

The number of District residents aged 65 and over is increasing each year. At the turn of the century there were 11,700; now there are 71,000, 6 times as many. During this same period the population has increased about 3 times.

There are many reasons for the growing number of senior citizens. Better private and public health care, better diets, and recreational programs have a tendency to increase the number of golden, productive years for many while problems have arisen for others. The latter group is of particular concern to the D. C. Department of Public Health, and it is gratifying to know that an increasing number of senior individuals are taking advantage of services of the Health Department as well as private medical facilities.

Included in the District's public health facilities are D. C. General Hospital, which provides comprehensive inpatient and outpatient medical treatment and care; Glenn Dale Hospital, a chronic disease hospital and rehabilitation center, serving those with chronic diseases and disabilities, including tuberculosis, and 4 geriatric clinics in public housing facilities.

At the present time some 1,500 patients are treated on a regular basis at 4 geriatric clinics (Arthur Capper, Garfield Terrace, Claridge, and the newly-opened Potomac Gardens).

The unified concept of treatment is the keynote of clinical operations. Physicians and staff members look at the patient as a whole, taking into consideration the interrelationship between the patient and his environment. Every effort is made to offer clinic patients the atmosphere of a private physician's office. Because patients come to the clinics on a regular basis they become familiar with the physician and staff members. Also, because of regular visits, subtle changes in the patient's condition can be noted and early treatment can be administered.

Because there is a growing realization that human problems are interrelated, social, physical and economic planning have been built into the pattern of treatment. In the District's program for the aged we are very much concerned about their mental outlook. Although the incidence of psychosis is not great, there is some evidence of depression. At the clinics we use group therapy with some success, utilizing the services of mental health workers. Sessions are held regularly at both Arthur Capper and Garfield Terrace Clinics, and plans are under way to increase psychiatric involvement in future programs.

In our dealing with senior citizens we have come to realize that problems of the aged cannot be separated from the total problems which confront our community. Thus, comprehensive community planning with the utilization of the resources of existing community organizations is used in meeting the total needs of citizens 65 years and older.

It has been said that services for the aged have been fragmented, reaching too few too infrequently, and that the efforts have been uncorrelated. This was a fair indictment until recent years in much of the country, including the District. Now, through the programs in our clinics and 2 hospitals, facilities and services are being expanded to meet the needs of a growing community of senior citizens.

This great challenge of geriatric services is being met daily through the coöperation of the men and women in private medical practice and by a host of voluntary organizations. As a team we are giving strength and hope to a group of citizens who were once shunted to the sidelines. They are now living useful, rewarding lives, but mostly we are giving them the feeling that they "belong."

Murray Grant, M.D., D.P.H.
*D.C. Director of Public Health*

KEOGH RETIREMENT PLANS

Individually Designed for Each Physician or
Partnership and Funded with Leading Mutual Funds
and Insurance Annuities in Major Companies

EUGENE F. ROESSER, C.L.U.

1130 Seventeenth Street, N.W.
Washington, D. C. 20036

District 7-1114

# Don't let monilia cut broad-spectrum therapy short...

# start with Tetrex-F®

## tetracycline phosphate complex-nystatin

Use of broad-spectrum antibiotics can cause fungal overgrowth in the alimentary tract... and give rise to symptoms so troublesome that therapy must be prematurely stopped. Tetrex-F (tetracycline phosphate complex-nystatin) helps you circumvent this problem.

The nystatin can prevent overgrowth of monilia; the phosphate complex delivers tetracycline to the blood rapidly. Side effects are infrequent.

**High-Risk Patients**

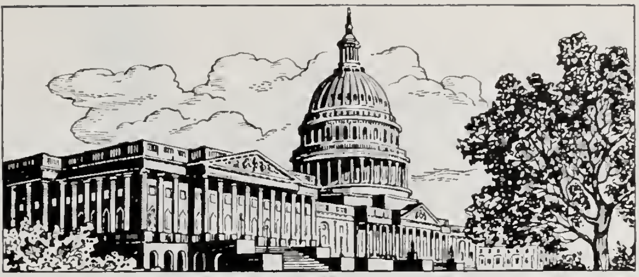
Tetrex-F (tetracycline phosphate complex-nystatin) is especially useful in patients most susceptible to fungal overgrowth during tetracycline therapy: (1) the elderly or debilitated, (2) young children, (3) the diabetic, (4) those on long-term tetracycline therapy, (5) those on steroid therapy, (6) those who have had moniliasis before, and (7) pregnant patients with a history of monilial vaginitis.

When you start with economical Tetrex-F (tetracycline phosphate complex-nystatin), you can complete the full course of broad-spectrum therapy with less chance of losing control elsewhere. A good start for a healthy finish.

PRESCRIBING INFORMATION. For complete information consult Official Package Circular. *Indications:* Infections of respiratory, gastrointestinal and genitourinary tracts and skin and soft tissues due to tetracycline-sensitive organisms, in patients with increased susceptibility to monilial infections. *Contraindications:* The drug is contraindicated in patients hypersensitive to its components. *Warnings:* Photodynamic reactions have been produced by tetracyclines. Natural and artificial sunlight should be avoided during therapy. Stop treatment if skin discomfort occurs. With renal impairment, systemic accumulation and hepatotoxicity may occur. In this situation, lower doses should be used. Tooth staining and enamel hypoplasia may be induced during tooth development (last trimester of pregnancy, neonatal period and childhood). *Precautions:* Bacterial superinfections may occur. Infants may develop increased intracranial pressure with bulging fontanels. In gonorrheal therapy, serologic tests for syphilis should be conducted initially and monthly for 3 months. *Adverse Reactions:* Glossitis, stomatitis, nausea, diarrhea, flatulence, proctitis, vaginitis, dermatitis, and allergic reactions may occur. *Usual Adult Dosage:* 1 capsule q.i.d. Continue for 10 days in Beta-hemolytic streptococcal infections. Administer one hour before or two hours after meals. *Supplied:* Capsules, bottles of 16 and 100. Each capsule contains tetracycline phosphate complex equivalent to 250 mg. tetracycline HCl activity and 250,000 units of nystatin. For Oral Suspension, 125 mg. tetracycline and 125,000 u. nystatin/5 ml., 60 ml. bottles.

BRISTOL

BRISTOL LABORATORIES
Division of Bristol-Myers Company
Syracuse, New York 13201



# NEWS & PERSONALS

## Summary of Executive Board Actions

### Proceedings of September 25 Meeting

Dinner for the Board members was served at 6:30 p.m. in the Exhibit Hall of the Medical Society. Dr. Karl C. Corley, Chairman, presided at the meeting. Present were Drs. Frank S. Bacon, C. Willard Camalier, Robert J. Coffey, Henry D. Ecker, Raymond T. Holden, William S. McCune, Edward W. Nicklas, Paul R. Wilner, and Mr. George W. Cooley, Secretary. The meeting was called to order at 7:10 p.m.

The minutes of the June 26 meeting were approved as mailed.

**Committee Meetings:** The Secretary reported that the following Committee meetings had been held since the last Board meeting:

| | | |
|---|---|---|
| June | 27 | Grievance Committee |
| | 27 | Committee on Medicolegal Problems |
| | 30 | Committee on Rehabilitation and Chronic Illness |
| July | 6 | Committee on Sports and Physical Fitness |
| | 13 | Ad Hoc Committee on Medical Licensure |
| | 13 | Traffic Committee |
| | 18 | Grievance Committee |
| | 26 | Finance Committee |
| August | 2 | Fee Review Committee |
| | 3 | Committee on Sports and Physical Fitness |
| | 4 | Committee on Child Welfare |
| | 10 | Traffic Committee |
| | 15 | Grievance Committee |
| | 24 | Committee on Aviation Medicine |
| September | 6 | Board of Credentials |
| | 7 | Fee Review Committee |
| | 7 | Committee on Environmental Health |
| | 12 | Committee on Medicolegal Problems |
| | 18 | Committee on Liaison with the Clergy |
| | 20 | Finance Committee |
| | 21 | Medical Bureau Committee |
| | 22 | Physician Placement Committee |
| | 22 | Committee on Public Information and Education |

**Board of Credentials:** On recommendation of the Board of Credentials, 12 applicants were elected to Active membership and 3 to Associate membership. Their names appear on page 704. Approval was also given to the following changes in membership status:

*Reinstatements*

*Active:* Elmer Wink Fugitt
*Associate:* William H. Wallop

*Transfers*

*Active to Associate:* Steven J. Conway, Alfred A. J. Den, and Arnold Charles Ratner
*Associate to Active:* Cesar M. Madarang, Narciso Anillo, and Lutgardo G. Panlilio

*Resignations*

*Associate:* Edward H. Bowen, Jr., Read N. Calvert, Arthur J. Linden, and William J. Mitchell
*Special:* Dorothy D. Dowd

Nominations to the Boards of Medical Service of D.C. and Group Hospitalizations, Inc., to become effective in April 1968, were considered but final determination postponed until the next meeting.

**Finance Committee:**

1. Consideration of a dues increase for 1968 was postponed until the October Board meeting.
2. A policy was adopted to offer $100 each year to each of the 3 D.C. medical school Student American Medical Association Chapters to help defray the expenses of a member attending the SAMA Annual Meeting.
3. Approval was given to continue membership ($100 annually) in "Aces and Deuces," an organization of states with 1 or 2 AMA delegates.
4. A request from the Greater Washington Citizens for Clean Air was referred to the Secretary for further clarification.
5. It was agreed to assist in publicizing the nonprofit agency, Chance for a Child, Inc., by distributing such information as is made available.

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6. Financial assistance to 2 members was reviewed and it was agreed to continue such assistance.

7. A request from the D. C. Dietetic Association for assistance in publicizing its program "Dial-a-Dietitian" was approved and a request for financial assistance referred to the Health Foundation of D.C.

**Committee on Public Information and Education:** A report on various public relations activities, including the daily TV and radio programs and plans for Community Health Week, was presented for the information of Board members.

**Items approved by mail:** Four items of business approved by mail were confirmed: (1) reorganization of the Regional Medical Programs Committee; (2) changes in committee structure; (3) the membership application of Dr. Carlos Silva; and (4) the President's nominees to the Nominating Committee.

**Society Awards:** The Committee on Public Information and Education recommended the following award recipients and they were approved by the Board: John Benjamin Nichols Award to the D. C. Society for Crippled Children and Mrs. George Hyman; Community Service Award to Margaret M. Kenrick, M.D.; and the Certificate for Meritorious Service to Edgar W. Davis, M.D.

**DOCPAC Request:** The previous policy regarding the inclusion of dues statements of other organizations with the mailing of Medical Society dues statements was reaffirmed.

**Medical Service of D. C.:** A letter from Dr. Everett J. Gordon protesting direct payment to patients by Medical Service of D. C. was discussed. The Secretary was instructed to ask Mr. George McGovern, Executive Vice President of Medical Service of D. C., to explain the contract provisions which require this method of payment.

**P.L. 89–97, Titles XVIII and XIX:** It was agreed to approve the recommendations of the Section on Internal Medicine calling for the use of Blue Cross-Blue Shield in implementing Title XIX of P.L. 89–97.

In reference to a letter from Dr. Murray Grant regarding a poll to determine the names of physicians who would serve patients under Titles XVIII and XIX of P.L. 89-97, under certain conditions, it was agreed that all such patients should have a free choice of physician and that a panel, however large, is not necessary; therefore, such a poll is not necessary. It was agreed that both groups of patients should be in the mainstream of medical care, with the same quality of medical care available to both.

### Other Business

Expenses were approved for Dr. Stanford Lavine's attendance, as Society representative, at the American Academy of Orthopedic Surgeons' Postgraduate Course on Sports in Oklahoma City, August 14–16, 1967.

It was reported that Dr. Harry Zehner, Jr. represented the Committee on Emergency Medical Services at a Conference on Problems of Prompt and Adequate Emergency Health Services, held in Washington, August 16–17, 1967.

Dr. Ecker reported on correspondence with Dr. Carl F. Hansen on his retirement as Superintendent of Public Schools in D. C.

It was agreed to coöperate with the AMA Volunteer Physicians for Vietman Program by urging members to participate.

Approval was given to the President's recommendation of Dr. William H. Cooper and Dr. S. Hazen Shea as potential replacements for Dr. Jerome F. Crowley on the Board of Medical Examiners in Medicine and Osteopathy.

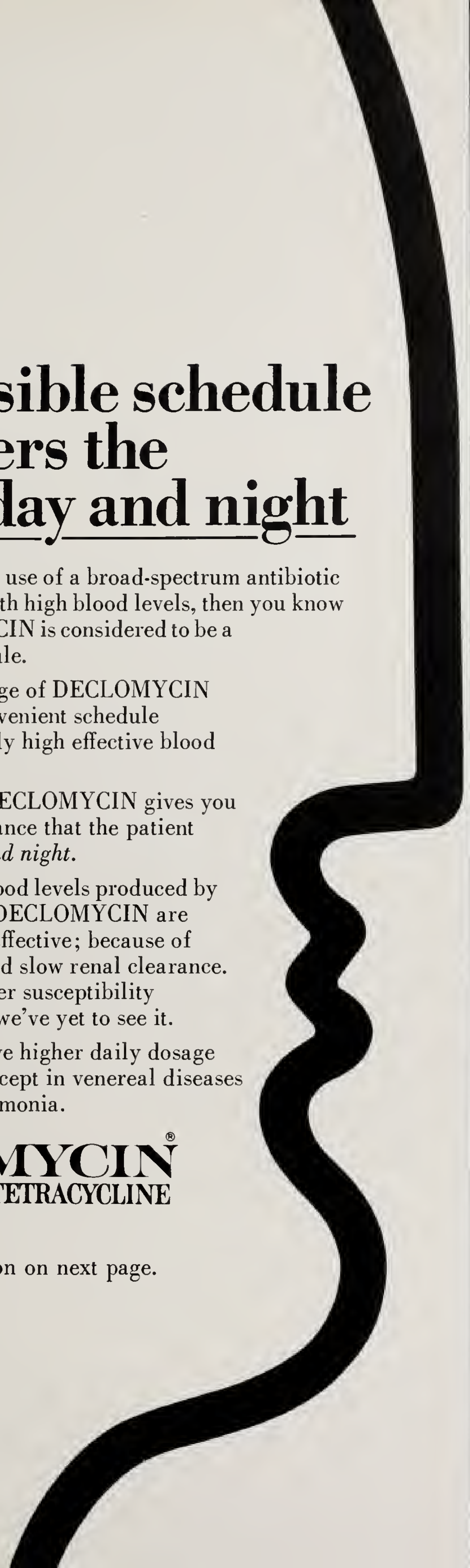
Confirmation was given to the nomination of Dr. Robert H. Barter to the AMA Committee on Scientific Assembly and of Dr. Naomi Kanof to the AMA Committee on Cutaneous Health and Cosmetics.

It was reported that the Society for Prevention of Blindness would use the Exhibit Hall for free testing of preschool-age children, October 1, 2 and 3.

Dr. Hyman Joseph Zimmerman was nominated as the Kober Lecturer for 1968.

Captain Bruce H. Smith, MC, USN, was approved as Consulting Editor of the Medical Annals, representing the Armed Forces Institute of Pathology, to succeed Major General Joe M. Blumberg, MC, USA.

There being no further business, the meeting was adjourned.



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**Precautions**—Overgrowth of nonsusceptible organisms may occure. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

**Side Effects**—Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes. A rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN. apparently dose related. Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth— dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs discontinue medication and institute appropriate therapy.

**Average Adult Daily Dosage:** 150 mg q.i.d. or 300 mg b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

In the treatment of syphilis a dosage schedule of a total of 12 to 18 Gm. given in equally divided doses over a period of 10 to 15 days should be followed. Close follow-up observation of the patient is recommended. including appropriate laboratory tests, since demethylchlortetracycline has not had adequate evaluation in all stages of syphilis. Spinal fluid examination should be included as part of this follow-up.

Acute gonococcal anterior urethritis in males has been treated effectively with a single dose of 600-900 mg. of DECLOMYCIN Demethylchlortetracycline. Individuals unable to tolerate large single doses due to gastrointestinal side effects may be treated with 150 mg. every 6 hours for a minimum of 4 doses or 300 mg. every 12 hours for a minimum of 2 doses. Females should be treated with a dosage of 150 mg. every 6 hours or 300 mg. every 12 hours until a cure is effected.

Primary Atypical Pneumonia (Eaton Agent): The average adult daily dosage is 900 mg. in 3 divided doses for six days.

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# Meetings

Approximately 2,800 physicians are expected to attend the **21st Clinical Convention of the American Medical Association** at the Astrohall, in Houston, November 26–29. The complete scientific program plus forms for advance registration and hotel accommodations were published in the October 23 issue of J.A.M.A.

In addition to the scientific programs arranged by the various sections of the AMA, there will be postgraduate courses on the following subjects: Fluid and Electrolyte Balance, Oncology, Cardiovascular Disease, and Obstetrics and Gynecology. There is no charge for these courses but registration is limited to 200 per course. There will also be Breakfast Roundtable Conferences on the following topics: Management of Cerebrovascular Insufficiency, Indication and Limitations of Uses of Antibiotics, the Moral and Ethical Aspects of Caring for the Dying Patient, Adolescence—Age of Rebellion—and Related Psychiatric Aspects. There will be the usual medical motion pictures and scientific and industrial exhibits in addition to some TV innovations.

**The Nineteenth Annual Regional Meeting of the American College of Physicians for the District of Columbia and Maryland** will be held in Baltimore on Saturday, December 2, in Gordon Wilson Hall on the eighth floor of the University of Maryland Hospital. A cordial invitation is extended to all Fellows and Associates of the College and to all physicians, residents and interns to attend.

The day will begin with Medical Grand Rounds at 9:00 a.m. Dr. Thomas W. Mattingly, Governor for the District of Columbia, will preside at the scientific session at 10:45 a.m., during which the following papers will be presented:

"An Evaluation of the Tissue Change Induced by Starvation and Caloric Restriction in Obesity," Drs. Michael F. Ball, L. H. Kyle, and J. J. Canary, of Georgetown University School of Medicine.

"Coronary Care in a Small Community Hospital without House Staff," Dr. Gerard Church and Lynda G. Kramer, R.N., Anne Arundel General Hospital, Annapolis, Md.

"The Lymphocyte in Immune Disease; the Nature of Its Memory of Antigenic Determinants," Dr. Thomas G. Shelton and Sahid Sanusi, M.S., of Howard University College of Medicine.

Luncheon will be served at the Holiday Inn at 301 West Lombard Street. Dr. James W. Haviland, a Regent of the College and Chairman of the Committee on Medical Services, will be the luncheon speaker. A charge of $4.00 per person is necessary to defray expenses for the luncheon.

Papers to be presented at the afternoon session, beginning at 2:00 p.m., are as follows:

"Endocrine and Histological Investigation of the Gynecomastia of Hyperthyroidism," Drs. Kenneth L. Becker, John L. Winnacker, Mary J. Matthews, and George A. Higgins, Jr., Veterans Administration Hospital, Washington, D. C., and George Washington University School of Medicine.

"Thrombotic Disease in Heart Patients Taking Oral Contraceptives," Dr. J. O'Neal Humphries, Johns Hopkins University School of Medicine.

"Hepatic Scanning in Amebic Liver Abscesses," Lt. Colonel Gerald S. Johnston, Lt. Colonel Thomas W. Sheehy, and Colonel Loren F. Parmley, Walter Reed Army Medical Center.

"Malaria in the United States: Its Increase and Treatment," Drs. David F. Clyde and Albert T. Dawkins, Jr., University of Maryland School of Medicine.

"Gold Therapy in Rheumatoid Arthritis: Reinstitution after Gold Dermatitis," Drs. Harry F. Klinefelter and H. E. C. Zheutlin, Johns Hopkins University School of Medicine.

"Hemostatic Defects in Infectious Diseases," Drs. Lewis H. Dennis and Marcel E. Conrad, Walter Reed Army Institute of Research.

"The Eight Hour Electrocardiogram," Dr. Bernard Tabatznik, Dr. Morton M. Mower, and Mr. William S. Staewen, Sinai Hospital, Baltimore.

Dr. John F. Maher, of Washington, and Dr. Alan Bernstein, of Baltimore, are Co-chairmen of the Program Committee.

Reservation cards and checks should be mailed to Dr. Richard B. Hornick, University Hospital, Baltimore, Md. 21201. Dr. Hornick is Chairman of the Committee on Arrangements.

**A Seminar on Chronic Respiratory Disease** will be held in the Exhibit Hall of the D. C. Medical Society building, Wednesday evening, January 10, and Thursday afternoon, January 11.

Participating in the program will be Dr. Oscar Auerbach, Senior Medical Investigator from the Veterans Administration Hospital in East Orange, New Jersey; Dr. Thomas Petty, Assistant Professor of Medicine, University of Colorado Medical Center in Denver; and Dr. Sol Katz, Chief of General Medical Services, Veterans Administration Hospital in Washington.

The 2-day program will provide an opportunity to discuss in small group sessions particular problems of diagnosis and treatment with specialists.

The Seminar is sponsored by the District of Columbia Thoracic Society, headed by Dr. Robert F. Donohoe. Dr. William J. Washington is Chairman of the Respiratory Disease Committee.

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**The First International Conference on Prematurity,** sponsored by the AMA Committee on Maternal and Child Care, will be held, January 11–13, 1968, at Pier 66 in Ft. Lauderdale, Florida.

An open invitation to attend is being extended to the Chairmen and members of all state and county Maternal and Child Care, Infant and Perinatal Mortality Committees; State Health Department Directors of Maternal and Child Health; medical school faculty members in Departments of Obstetrics, Pediatrics, Preventive Medicine and Public Health. Other physicians and representatives of groups interested in the problems of prematurity are cordially invited to attend.

Those interested in receiving additional information about registration for this Conference are requested to write to Mr. Wesley J. Duiker, Secretary, Committee on Maternal and Child Care, American Medical Association, 535 North Dearborn Street, Chicago, Illinois 60610.

## General News

The Dean of Georgetown University School of Medicine extends a cordial invitation to all members of the Medical Society of D. C. to attend the **Conferences in Diagnosis and Treatment** given by the faculty of **Georgetown School of Medicine** during the academic year 1967–1968. These conferences are held twice weekly, on Wednesdays, from 3:45 to 5:15 p.m., in the Gorman Auditorium, and on Saturdays, from 9:00 to 10:30 a.m. and from 10:45 a.m. to 12:15 p.m., in Room 102 of the Medical School Building. There is no charge.

**Howard University College of Medicine** has joined the Georgetown and George Washington University Schools of Medicine in the use of educational facilities at Children's Hospital for the training of medical students in pediatrics. A contract signed with Howard, paralleling agreements with Georgetown and George Washington, recognizes that the Hospital and the Universities ". . . are each organized to fulfill certain essential and related functions in community medical care, education and research. . . ." The agreement with Howard was formalized, September 19, at a meeting of the Hospital-University Committee. This is the joint committee, consisting of medical school and Hospital officials, which initiates policy dealing with the teaching of medical students at the Hospital.

Under an agreement between **Georgetown University and Holy Cross Hospital** of Silver Spring, Md., the University's School of Medicine will sponsor **20 seminars** during 10 months, excluding July and August. "The purpose of these conferences is to bridge the gap between new knowledge learned in laboratories and its application to patient care in a community hospital," said Dr. Bruce I. Shnider, Associate Dean of the School of Medicine. "Faculty members from our school will make available to the Holy Cross staff the most recent results of research."

Conferences on obstetrics-gynecology are held from 8:00 to 9:30 a.m. and on pediatrics from 8:00 to 9:30 p.m., once a month at Holy Cross. The sessions began September 13.

A major new national voluntary health organization, **the Epilepsy Foundation of America,** represents the merging of 2 national organizations concerned with epilepsy, the Epilepsy Association of America and the Epilepsy Foundation. Negotiations for a merger have been going on for about 4 years. The agency's national headquarters will be in Washington, D.C. at 1419 H Street, N.W. An office in New York City will also be maintained. The existing chapters of both organizations will continue as chapters of the new organization. Mr. Neal Gilliatt, Chairman of the Board of Interpublic, Inc., is the first President of the organization.

**The Royal Society of Medicine Foundation, Inc.** has been formed to establish closer relations between members of the medical professions in Great Britain and the United States. Organized under the auspices of The Royal Society of Medicine, the Foundation provides an opportunity for individuals, corporations, government agencies, and charitable foundations in the United States to support medical research in Great Britain. Tax-deductible contributions to the Foundation will be used to improve facilities for medical research and education as well as to provide medical scholarships, to sponsor conferences for the exchange of information on medical research, and to preserve medical literature.

The Royal Society of Medicine was organized in London in 1805. It has a membership of 13,000, including over 1,000 U. S. physicians. Among its principal activities is the maintenance of one of the largest medical libraries in the world and the most comprehensive one outside the United States.

The Board of Directors of the Foundation is comprised of eminent leaders in the fields of medicine and business in Great Britain and the United

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States. One of the Board members is Dr. William S. Middleton, Professor of Medicine and Dean Emeritus of the University of Wisconsin School of Medicine and an Honorary member of the D. C. Medical Society.

With a $25,000 **grant to Georgetown University**, the Christian Family Movement has become the first Catholic lay organization to support a basic research facility in human reproduction. The grant, announced September 21, was awarded to the Department of Obstetrics and Gynecology in the School of Medicine. The research program will be directed by Dr. Paul D. Bruns, Professor and Chairman of the Department, and Dr. Andre Hellegers, Professor of Obstetrics and Gynecology. The funds will be used to build an extension to the research facility housing laboratory animals, laboratories and operating rooms.

Officers serving the **Section on Otolaryngology of the Medical Society of the District of Columbia** for 1967–68 are:

Dr. Joseph Sabri, *Chairman*; Dr. Louis B. Balla, *Vice Chairman*; Dr. I. Sidney Jaffee, *Secretary*; and Dr. Blair Webb, *Treasurer*.

The following physicians have been elected officers of the **Washington Orthopedic Club** for the current year:

Dr. Charles H. Epps, *President*; Dr. Robert Spicer, *Vice President*; and Dr. Leo B. VanHerpe, *Secretary-Treasurer*.

The 1967–68 officers of the **Woman's Auxiliary to the Medical Society of the District of Columbia** assumed their duties on June 1. They are:

President: Mrs. James H. Scully
President-elect: Mrs. Alfred J. Suraci
First Vice President: Mrs. Joseph M. Daly
Second Vice President: Mrs. James E. Wissler
Recording Secretary: Mrs. Paul Jaquet
Assistant Recording Secretary: Mrs. Joseph P. Swift
Corresponding Secretary: Mrs. John Fox
Assistant Corresponding Secretary: Mrs. Paul C. Adkins
Treasurer: Mrs. George H. Crofton
Assistant Treasurer: Mrs. George W. Hyatt

**Mrs. Mary Cooley** has been named **Executive Director of the Washington Heart Association,** succeeding Miss Beatrice Hodgson, who retired, September 30, after more than 18 years with the organization. Dr. Jack Kleh, President of the Association, announced Mrs. Cooley's appointment to the position, effective October 1. Mrs. Cooley was formerly a medical social worker with Northwestern University Evanston Hospital. She has been with the Washington Heart Association since April, 1963, most recently as Program and Research Director. A graduate of the University of Cincinnati, she has done graduate work there as well as at the Universities of Toledo and Michigan.

**Dr. Lawrence A. Smookler,** of San Francisco, California, is the **new Field Director of the American Medical Association's Volunteer Physicians for Vietman program.** Dr. Malcolm E. Phelps, who recently retired as Field Director, was elected Vice President of the AMA at the Association's Annual Convention in Atlantic City in June.

**A handy reference book** for looking up various **U. S. Post Office zip code numbers,** suitable for home and office use, may be ordered from the Zip Code Publishing Company, Inc., 7426 West Capitol Drive, Milwaukee, Wisconsin 53216. Containing over 35,000 zip codes, this compact directory is priced at $1.00 plus 25 cents for handling and postage.

Some new publications are available from the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C. 20402.

**"Education for the Allied Health Professions and Services"** (PHS Publ. No. 1600): This report covers trends in the supply of health manpower as well as the needs, current educational programs and their output, and recommendations of the Allied Health Professions Educational Subcommittee of the National Advisory Health Council to the Surgeon General of the Public Health Service. Single copies are available free from the Bureau of Health Manpower, PHS, 800 North Quincy Street, Arlington, Va. 22203. Copies may be purchased from the Government Printing Office for 45 cents each.

**"Drugs vs. Cancer"** (PHS Publ. No. 1652): A 17-page report on the current status of cancer chemotherapy research, this is the third in a Research Report series prepared by the Research Information Branch of the National Cancer Institute. The first in the series was "Progress Against Leukemia," published in 1962; the second, "Virus-Cancer Research," was issued in 1964. Single copies of "Drugs vs. Cancer" are available without charge from the Public Health Service, Washington, D. C. 20201. The pamphlet is availble in quantity from the Superintendent of Documents at 15 cents per copy.

The following leaflets in the health information series for international travel were revised in May 1967 and may be purchased from the Superintendent of Documents for 5 cents each or $3.75 per hundred copies.

**"Health Information for Travel in Europe"** (PHS-748)

**"Health Information for Travel in Mexico, Central and South America, and the Caribbean"** (PHS-748B). Since the revision of this pamphlet smallpox vaccination is no longer required for persons traveling between the United States and Mexico provided they have visited only in these 2 countries during the preceding 14 days.

**"Health Information for Travel in Asia, Including Japan, Indonesia, the Philippines, and in Australia and New Zealand"** (PHS-748C)

**"Health Information for Travel in Africa, Including Malagasy Republic and Neighboring Islands"** (PHS-748D)

Previous issues of these leaflets should be destroyed because of changes in typhoid, tetanus, diphtheria, poliomyelitis, and plague vaccinations.

## Personals

**Dr. Robert H. Barter,** Professor of Obstetrics and Gynecology at George Washington University School of Medicine, has been invited to give the biennial Anglo-American Lecture on Infertility before the Royal College of Obstetricians and Gynecologists in London in May 1968. He is the third person so honored.

Dr. Barter recently relinquished the chairmanship of the Department of Obstetrics and Gynecology at George Washington University but continues his professorship in the Department. He has opened offices for the practice of his specialty in the University Medical Building at 2141 K Street, N.W.

**Dr. William B. Walsh,** founder and President of Project HOPE, was the recipient of 4 new honors during the month of October. They were: The Americas Award, presented October 12 in New York City by The Americas Foundation, Inc.; the Distinguished Service Award of the American Medical Authors, also in New York, October 23; and the Theodore Roosevelt Distinguished Service Medal, presented October 27, in Washington, D. C. On October 29, in Washington, D. C., the International College of Dentists conferred upon him Honorary Fellowship "in recognition of outstanding contributions to the dental profession and its public appreciation."

**Dr. William W. Funderburk,** of Freedmen's Hospital, has volunteered for a 60-day period of service with the AMA Volunteer Physicians for Vietnam. He left the States on October 6 and plans to be gone until December 7. Dr. Funderburk is Assistant Professor of Surgery at Howard University College of Medicine.

**Dr. Irving B. Brick,** Professor of Medicine at Georgetown University School of Medicine and Director of the Division of Gastroenterology at Georgetown University Hospital, has been appointed Acting Chairman of the Department of Medicine, effective September 1. He replaces Dr. Laurence H. Kyle, who is taking a sabbatical year in order to work in the Department of Metabolism at St. Vincent's Hospital in Dublin, Ireland.

**Dr. Allen S. Cross,** Chief of Health and Examining of the D. C. Department of Public Health, **and Dr. Victor H. Esch,** of the D. C. Board of Police and Fire Surgeons, received Graduate Certificates of the Committee on Injuries of the American Academy of Orthopaedic Surgeons for completing the Advance Course of Instruction on Initial Emergency Care and Transportation of the Sick and Injured. The 3½-day course was sponsored by the Committee, September 6–9, at the Harvard Graduate School of Business Administration in Boston.

Enrolled were ambulance attendants, policemen, firemen, public health, civil defense and other officials, totaling 225 registrants, from Boston and 130 other cities. The advanced training was given to improve the skills and knowledge of persons involved in the emergency handling of critically sick and injured persons.

Dr. Warren D. Brill, Chairman of the Committee on Public Information and Education, has asked that recognition be given to those members of the D. C. Medical Society who served as **judges for the 24th Annual Science Fair,** held April 18, 1967 at the D. C. National Guard Armory. They were: Drs. Carlton P. Alexis, Arthur S. Bresler, A. J. Connolly, Edward E. Cornwell, Jr., Orville W. Donnelly, Michael J. Halberstam, Jean L. Harris, William E. Matory, Samuel B. Rosser,

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Mitchell W. Spellman, and Warren J. Strudwick. Dr. Lewis H. Kurtz, Chairman of the Medical-Science Judging, stated that the Science Fair Committee, as well as the students, seemed pleased with the judges' decisions.

**Dr. Roland B. Scott,** Chairman of the Department of Pediatrics at Howard University College of Medicine, was in Brazil during August on a visit and lecture tour. Following a lecture before the Brazilian Pediatric Society in Rio de Janeiro he was made an honorary member of the Society and awarded a diploma by its President, Dr. Athayde Fonseca. In the same city he addressed the staff of the Hospital Estadual Jesus, where Dr. Fonseca is Chief of the Pediatric Service. Dr. Scott was a guest of the Department of Pediatrics at the University of Sao Paulo. He also visited the new capital city of Brasilia where he consulted with leading pediatricians and lectured before their hospital staffs.

## Patients Needed at Clinical Center

The coöperation of physicians is requested in the referral of patients for a study of chylous ascites being conducted by the Metabolism Branch of the National Cancer Institute at the Clinical Center of the National Institutes of Health in Bethesda, Md.

Of interest are patients with chylous effusions including those with effusions secondary to congenital lymphatic abnormalities, trauma, localized or diffuse retroperitoneal disease (including pancreatitis), and neoplasm. Studies will be directed at determining the relationship of ascites to lymphatic abnormalities, immunological defects, serum protein deletion, and protein-losing gastroenteropathy.

Selected patients will be admitted to the Clinical Center and receive full diagnostic workup. Upon completion of their studies patients will be returned to the care of the referring physician, who will receive a full report of the studies done. Where possible recommendations for therapy will also be made available to the referring physician.

Physicians interested in having their patients considered for admission to this study may write or telephone Dr. Warren Strober or Dr. Thomas A. Waldmann, Clinical Center, Room 4-N-110, National Institutes of Health, Bethesda, Md. 20014; telephone: 656-4000, Ext. 66480.

# Correspondence

Boston, Mass., September 20, 1967

To the Editorial Board:

The recognition given Dr. Wallace Yater on the completion of 35 years of service as Editor of the Medical Annals of the District of Columbia is known by readers of the publication to be well deserved. His creative leadership in the establishment of a medical journal for the District Society in 1932 and his skilled editorial guidance year after year since then have brought about its undoubted success.

As one who was associated with Wallace Yater when he was at the Mayo Clinic for graduate training in internal medicine, I recall that he was no ordinary fellow or resident. Already he had taken the first steps in his career as medical educator and author; he had held a professorship in his medical school and co-authored a textbook (Barton and Yater: Symptom Diagnosis). He soon demonstrated the all-round ability that led to offers to remain in Minnesota as a member of the Mayo staff. He chose, however, to return to his home environment. In Washington he continued to exhibit his talents as professor of medicine, author, practicing physician, and leader in medical organizations, local and national. His breadth of experience in these varied roles plus his literary skill have given him ideal qualifications for his editorial tasks.

Dr. Yater's friends everywhere share with the members of the Medical Society of the District of Columbia pride in his record service as medical editor. It is believed that no other medical journal has been headed by one individual for 35 years. Congratulations to the Dean of Medical Editors!

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Butazolidin®, phenylbutazone
In Acute Superficial Thrombophlebitis

Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently. Large doses of Butazolidin alka are contraindicated in glaucoma.

Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage occur. Make regular blood counts. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

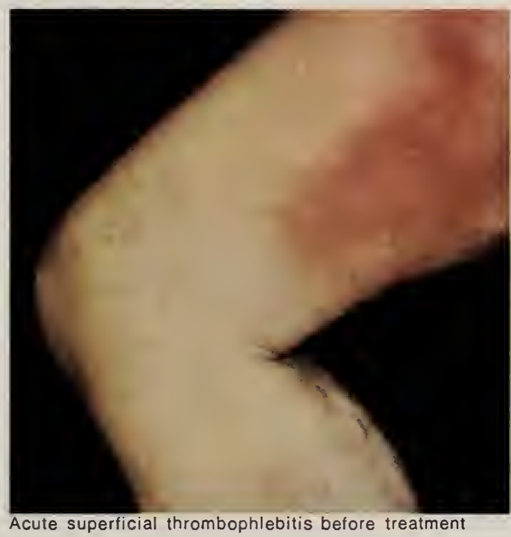
Adverse Reactions: The most common are nausea, edema and drug rash. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately before or after meals or with milk to minimize gastric upset. Mild drug rashes frequently subside with reduction of dosage. However, rash accompanied by fever or other systemic reactions usually requires withholding medication. Purpuric rash has also been reported. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, or a generalized allergic reaction similar to serum sickness may occur and require permanent withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

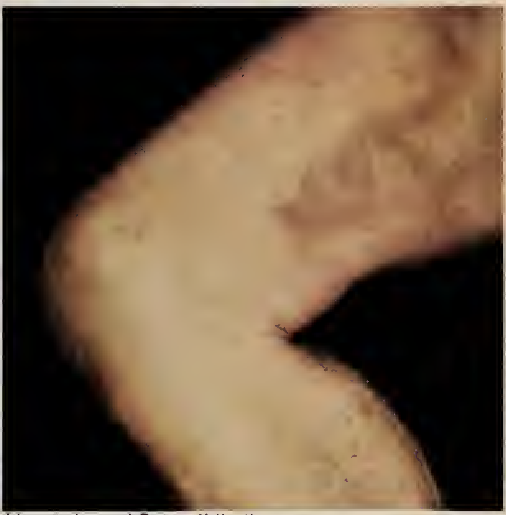
Dosage in Acute Superficial Thrombophlebitis: Initial: 6 capsules or tablets daily in divided doses for 2 or 3 days. Maintenance: 3 capsules or tablets daily. Usual duration of therapy is 5 to 7 days (rarely beyond 10 days). 6509-V(B)R2

*Stein, I.D.: Presented at the American Academy of General Practice, Dallas, Sept. 1967.

**For complete details, please see full**

# it used to take weeks


Acute superficial thrombophlebitis before treatment


After 5 days of Butazolidin therapy

In acute superficial thrombophlebitis, patients were usually bedfast for 2 to 4 weeks, tying up hospital beds, requiring costly nursing care and time-consuming procedures such as warm soaks and packs.

When Butazolidin was added to the usual regimen, 960 of 1000 patients obtained complete resolution; most required only 30 capsules or tablets; relief of pain and discomfort and regression of inflammatory signs and fever occurred within a few days.*

Side effects occurred in 6% of the 1000 patients. While none were serious or long-lasting, Butazolidin can produce severe side effects in rare instances. Further, not every patient can take Butazolidin. Therefore, select patients with care and follow them closely. Contraindications, Warning, Precautions and Adverse Reactions are summarized in adjacent column.

Butazolidin gets bedfast thrombophlebitics out of bed, fast. Usual duration of treatment is 5 to 7 days, and rarely exceeds 10 days. Try it and see. For full details, please refer to the complete prescribing information.

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Capsules:
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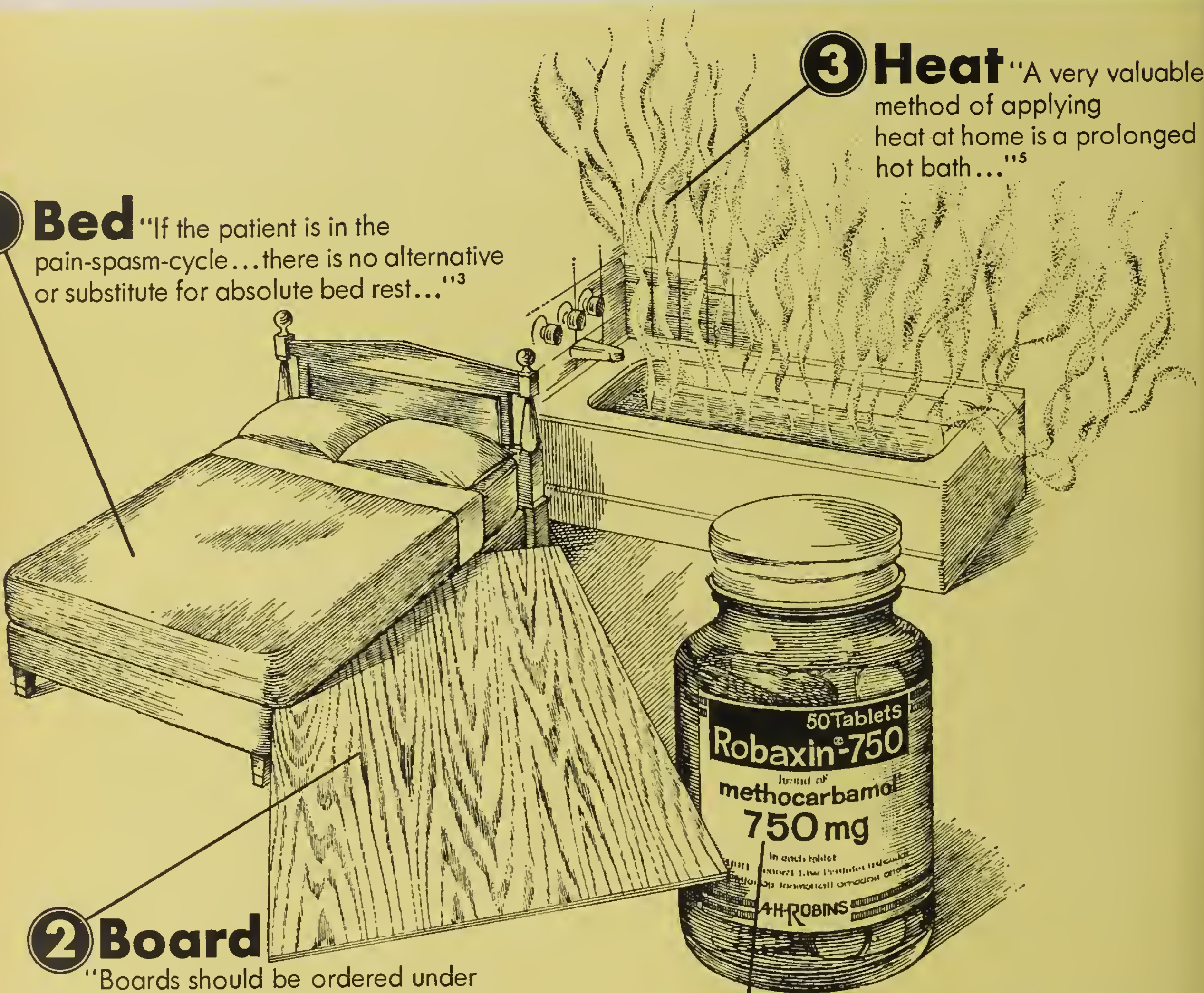
**The low back pain that is most frequently seen in general practice is mechanical in nature, i.e., postural back pain, joint dysfunction and acute back strain.[1,2] For this type of discomfort, a conservative regimen is usually sufficient to relieve aches and pains, and to help keep the patient functioning. Components of this basic program include:**



**① Bed** "If the patient is in the pain-spasm-cycle... there is no alternative or substitute for absolute bed rest..."[3]

**② Board** "Boards should be ordered under the mattress... these boards act by immobilizing the spine..."[4]

**③ Heat** "A very valuable method of applying heat at home is a prolonged hot bath..."[5]

**④ Robaxin®-750** (methocarbamol, 750 mg. capsule-shaped tablets) A well-tolerated[6] skeletal muscle relaxant, methocarbamol helps relieve spasm "...without interfering with normal tone and movement."[7] And there is little likelihood of sedation.[6]

**Indicated** for relief of skeletal muscle spasm. **Contraindicated** in hypersensitive patients. **Side Effects** (lightheadedness, dizziness, drowsiness, nausea) may occur rarely, but usually disappear on reduced dosage. Hypersensitivity reactions develop infrequently. See product literature for further details. **Also available:** Robaxin® Tablets (methocarbamol, 500 mg.) Robaxin Injectable (methocarbamol, 1 Gm./10 cc.) **References:** (1). Godfrey, C.M.: Applied Therap. *8*:950, 1966. (2). Gottschalk, L.A.: GP *33*:91, 1966. (3). Rowe, M.L.: J. Occup. Med. 2:219, 1960. (4). Cozen, L.: South Dakota J. Med. *18*:26, 1965. (5). Soto-Hall, R.: Med. Sc. *14*:23, 1963. (6). Weiss, M. and Weiss, S.: J. Am. Osteopath. A. 62:142, 1962. (7). Feuer, S.G., *et al.*: New York J. Med. 62:1985, 1962.

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# Obituaries

## Louis Samuel London, M.D.

(1883–1967)

Dr. Louis S. London, who practiced psychiatry in New York City and Washington for many years, died in Miami, July 16, 1967. Retired from practice a number of years ago, he had last made his home in Coral Gables, Florida.

Dr. London was born in Russia, February 25, 1883. He spent his early years in New York City and graduated in medicine from the Long Island College Hospital in 1908. He interned at the New York City Children's Hospital for a year, 1909–1910.

During a long practice, Dr. London was staff physician at several Federal and state hospitals: Central Islip State Hospital, Long Island, 1911–1918; Manhattan State Hospital, 1920–1921; U. S. Public Health Service and Veterans Bureau, 1921–1927.

In 1927 and 1932 he went to Vienna for postgraduate study in psychiatry and psychoanalysis.

He was licensed to practice in the District of Columbia in 1933. Earlier he had served on the staff of St. Elizabeths Hospital for a year.

Elected to Active membership in the Medical Society of the District of Columbia in 1940, he became a Life member in 1965. He was a member of the American Medical Association, the American Psychiatric Association, the New York Society of Clinical Psychiatry, St. Elizabeths Hospital Medical Society, and member and Past President of the Washington Society for the Advancement of Psychotherapy. He was a diplomate of the American Board of Psychiatry and Neurology and the author of several books in his field.

Surviving is a daughter, Mrs. Harold M. Stern, 6011 Emerson Street, Bladensburg, Md.

## Montgomery Earle Higgins, M.D.

(1879–1967)

Dr. Montgomery E. Higgins, retired Naval medical officer, died, September 28, 1967, at the Bethesda Naval Medical Center. He lived at 2610 Weller Road, Wheaton, Md.

Dr. Higgins was born at Sir Johns Run, West Virginia, October 29, 1879. He graduated in medicine from George Washington University in 1904. After interning at Garfield Memorial Hospital for a year he served a residency at Ancon Hospital in the Canal Zone, Panama, from 1905 to 1907. He did graduate work in Vienna and Paris, at the London School of Tropical Medicine, and at Harvard Medical School.

His 38 years of active duty with the Navy included service as a surgeon at Naval Headquarters in Paris in 1929 and surgeon with the Asiatic Fleet from 1931 to 1934. He came back to Washington in 1942 and was retired from active duty with the rank of Captain in 1943.

Dr. Higgins taught tropical medicine at George Washington University School of Medicine on several of his tours of duty in Washington. Until 5 years ago he practiced medicine in offices at 1150 Connecticut Avenue, N.W.

He was a Fellow of the American College of Surgeons and the American Academy of Tropical Medicine. He was first elected to Associate membership in the D. C. Medical Society in 1923. From then until 1960 he was intermittently a member while stationed in and near Washington. He was a member of the Army-Navy Club and the Chevy Chase Country Club. Earlier he had been a member of the Cosmos Club.

He leaves his wife, Mrs. Grace Young Higgins, and a son, Montgomery Higgins.

## Gerald Arthur Hopkins, B.S., M.D.

(1901–1967)

Dr. Gerald A. Hopkins, who retired, September 1, from the staff of the Washington Hospital Center, died, September 12, 1967, at the Ohio Valley General Hospital in Wheeling, W. Va. He lived at 5600 Springfield Drive, Bethesda, Md.

Dr. Hopkins was born in Corry, Pa., November 28, 1901. He graduated in science and medicine from the University of Cincinnati College of Medicine, receiving his medical degree in 1929. He interned for a year at Garfield Memorial Hospital in Washington, D. C.

Dr. Hopkins joined the Navy in 1940 with the rank of Lieutenant Commander. His early assignments included duty at the Naval Gun Factory Dispensary and the Naval Medical Center in Bethesda. He served aboard the military transport, *U.S.S. Pinckney* in the Pacific area during World War II. After the War he became Senior Medical Officer at the Portsmouth (N.H.) Naval Yard, and later at the Boston Naval

Shipyard. He retired as Captain in 1960 after 20 years of service.

He was an Active member of the Medical Society of the District of Columbia from 1931 to 1946. He was reëlected an Active member when he returned to the District in 1960, and transferred to Associate status in 1961.

His wife, the former Annie Marie Clancy, died early this year. He leaves his mother, Mrs. Harry V. Hopkins, of Conneaut, Ohio; a daughter, Miss Mary Ann Hopkins, of Wheeling, W.Va.; 2 brothers, David G., of Sturgis, Mich., and Harry V., of St. Petersburg, Fla.; and 3 sisters, Mrs. Walter Brown of Conneaut, Ohio, Mrs. Robert Warren of Wheaton, Md., and Mrs. Donald Heddon of Scottsdale, Ariz.

### Medical Genetics—Bartalos

(*Continued from page 656*)

examples of this approach. It is also possible to supply metabolites in the diet when production is impaired and when absence has clinical consequences. This is practiced in genetic defects of thyroid hormonogenesis by supplementation of thyroid hormone.

These examples of therapeutic approaches which are based on the biochemical characteristics of the genetic defect represent a beginning. We can expect further developments in this area as more and more data accumulate on the biochemical characteristics of genetic diseases in man.

Presently available therapeutic approaches are directed to gross bodily features and to the processes of intermediary metabolism. Although further advances in these fields are certain, search is going on for new therapeutic measures. These are still in the early experimental stage and involve the modification of protein synthesis and of the genetic material proper. Studies in these areas may lead to major breakthroughs soon.

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### Thalassemia Syndromes and Hemoglobinopathies—Verly et al

(*Continued from page 669*)

#### Summary

We examined 1,506 individuals aged 3 to 17 years by hematologic and chemical methods for the detection of thalassemia syndromes and other hematologic disorders. The incidence of the major findings in this Negro population was as follows: abnormal hemoglobins (S and C), 7.62 per cent; iron-deficiency anemia, 4.78 per cent; and thalassemia syndromes, 3.18 per cent.

Our study suggests that the mutant genes for thalassemia are not rare in North Americans of African descent.

At present there is no single finding or test that establishes a diagnosis of thalassemia. The criteria for identification of the various thalassemia states are based on hematologic and chemical studies of parents, siblings, and other close relatives.

The authors acknowledge the technical assistance of Mr. Melvin L. Seard, Mrs. Emeline Wynter, and Mrs. Mary Wilkins of the hematology laboratory staff.

#### References

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## Diagnosis:

**cystitis?**
**pyelonephritis?**
**pyelitis?**
**urethritis?**
**prostatitis?**

in any case,
usually gram-negative*

## Therapy:

two 500 mg. Caplets® q.i.d.
(initial adult dose)

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a specific anti-gram-negative

eradicates most urinary tract infections...

- Low incidence of untoward effects; no fungal overgrowth, crystalluria, ototoxic or nephrotoxic effects have been observed.
- "Excellent" or "good" response reported *in more than 2 out of 3* patients with either chronic or acute gram-negative infections.[1]

*As many as 9 out of 10 urinary tract infections are now caused by gram-negative organisms: E. coli, Klebsiella, Aerobacter, Proteus, Paracolon or Pseudomonas[2]... However, infections of the urethra and prostate caused by non-gonococcal gram-negative organisms are believed to be less prevalent.

**Indications:** Urinary tract infections caused by gram-negative and some gram-positive organisms.

**Side effects:** Mainly mild, transient gastrointestinal disturbances; in occasional instances, drowsiness, fatigue, pruritus, rash, urticaria, mild eosinophilia, reversible subjective visual disturbances (overbrightness of lights, change in visual color perception, difficulty in focusing, decrease in visual acuity and double vision), and reversible photosensitivity reactions. Marked overdosage, coupled with certain predisposing factors, has produced brief convulsions in a few patients.

**Precautions:** As with all new drugs, blood and liver function tests are advisable during prolonged treatment. **Pending further experience, like most chemotherapeutic agents, this drug should not be given in the first trimester of pregnancy. It must be used cautiously in patients with liver disease or severe impairment of kidney function.** Because photosensitivity reactions have occurred in a small number of cases, patients should be cautioned to avoid unnecessary exposure to direct sunlight while receiving NegGram, and if a reaction occurs, therapy should be discontinued. The dosage recommended for adults and children should not arbitrarily be doubled unless under the careful supervision of a physician. Bacterial resistance may develop.

When testing the urine for glucose in patients receiving NegGram, Clinistix® Reagent Strips or Tes-Tape® should be used since other reagents give a false-positive reaction.

**Dosage: Adults: Four Gm. daily by mouth (2 Caplets® of 500 mg. four times daily) for one to two weeks. Thereafter, if prolonged treatment is indicated, the dosage may be reduced to two Gm. daily. Children may be given approximately *25 mg. per pound* of body weight per day, administered in divided doses. The dosage recommended above for adults and children should not arbitrarily be doubled unless under the careful supervision of a physician. Until further experience is gained, infants under 1 month should not be treated with the drug.**

**How supplied:** Buff-colored, scored Caplets® of **500 mg. for adults**, conveniently available in bottles of 56 (sufficient for one full week of therapy) and in bottles of 1000. **250 mg. for children**, available in bottles of 56 and 1000.

**References:** (1) Based on 23 clinical papers, 1512 cases. Bibliography on request. (2) Bush, I. M., Orkin, L. A., and Winter, J. W., in Sylvester, J. C.: Antimicrobial Agents and Chemotherapy—1964, Ann Arbor, American Society for Microbiology, 1965, p. 722.

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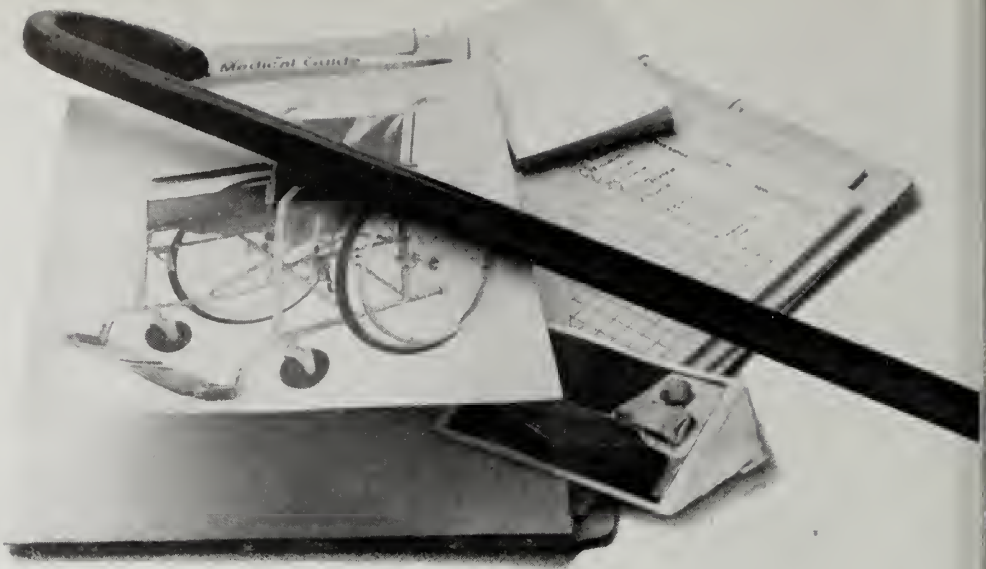

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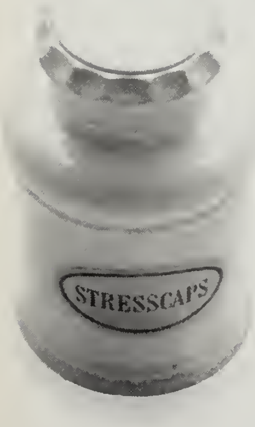

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| Vitamin $B_1$ (as Thiamine Mononitrate) | 10 mg |
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# BOOK REVIEWS

**Cecil-Loeb Textbook of Medicine,** 12th ed. Edited by Paul B. Beeson, M.D., and Walsh McDermott, M.D. Price, $20.50; 2-volume set, $24.50. Pp. 1738, illustrated. Philadelphia: Saunders, 1967.

Cecil-Loeb's Textbook of Medicine is now 40 years old and appears this year in its twelfth edition. Perhaps not as handsomely bound as one of its competitors, it otherwise is similarly available in either a single volume or in a 2-volume set (the calculated risk of owning a 2-volume set is that the wrong one will be reached for about half the time). The single volume seems to be handy enough. Through the miracles of using thinner paper, tighter printing, and other space-conserving devices, the single volume is almost 2 pounds lighter and 5/8 of an inch slimmer than the previous edition. It also contains more information in fewer pages.

There appears to be little in the way of omissions for a reference text of the scope of this venerable and familiar book. The editors point out that 57 new subjects are discussed since the eleventh edition, and several sections have undergone invigorative transformation. I notice that Bangungut isn't mentioned in the index (it may not deserve to be), but as evidence that it is otherwise as comprehensive and up-to-date as can reasonably be expected of any textbook on the day of publication, there are brief observations on such modern problems as LSD intoxication and chloroquine-resistant falciparum malaria.

This new twelfth edition is a reliable, informative and important addition to any medical library.

George A. Tralka, M.D.

**Synopsis of Pediatrics,** 2nd ed. James G. Hughes, B.A., M.D., with 26 collaborators. Price, $10.85. Pp. 1099, with 86 illustrations. St. Louis: Mosby, 1967.

This book is indeed a masterpiece of condensation. It is quite remarkable how, in spite of the necessary distillation of material, the residue is presented in an utterly readable form, and one does not experience the usual frustration induced by the traditional Manual of Pediatrics.

Dr. Hughes has called upon 26 colleagues from the faculty of the University of Tennessee College of Medicine to collaborate with him in this endeavor. One immediately has the picture of a most active and versatile Department of Pediatrics, with many high quality resources in other parts of the medical school.

Although not a large volume, the book is too heavy to be included in the average white coat pocket, where it would be of great value. The print is clear, and the single column format easy to read. Illustrations are generously provided in the form of photographs, diagrams and charts. The table of drug dosages has been adapted from a similar scheme by H. C. Shirkey in Nelson's Pediatrics, but in many instances there is a more detailed description of the therapy under the individual disease. The index is most adequate, providing a quick guide to the answer and not a bewildering distraction at a moment of uncertainty. The editing, professional and literary, has been most efficient. The style in thinking and expression is easy and straightforward, and the transition from one author to another occurs without difficulty. As fitting to the general purpose of the book, there is little attempt to provide references except where the sources of material used are directly quoted. The latter are usually from standard American textbooks in pediatrics.

It is noteworthy that the second edition of this book has been published just 4 years after its first appearance. To be of value, a work of this kind will need constant revision and updating. Of interest too is the fact that a Spanish edition has already been released. It would seem that this book would have great appeal in countries where much of pediatrics is practiced by physicians without formal training in the specialty.

Current recommendations of the Academy of Pediatrics are endorsed in areas such as immunizations and nutrition.

The subject matter is covered in 27 chapters, which are devoted to such general topics as psychological aspects of childhood, accidents in childhood, and mental retardation, and also to the more usual systematic review of the pathology of disease entities.

The problems of sex differentiation and development are clearly described. Twenty pages are devoted to an introduction to autosomal abnormalities, and the presentation of current concepts is again extremely pertinent for the physician with limited time for reading literature about matters which do not concern him directly.

The chapter on Cancer in Childhood has been completely rewritten in this edition. In 10 pages, neuroblastoma, retinoblastoma, Wilms' tumor, rhabdomyosarcoma, Hodgkin's disease, lymphosarcoma, and bone tumors are all adequately covered. Leukemia and brain tumors are discussed in chapters relating to the systems involved.

The present status of tuberculosis is well described. Special reference should be made to the description and comparison of currently acceptable methods of skin testing, which is very timely. However, some reference to the incidence and age distribution of tuberculosis in this country would have been an acceptable addition.

Dr. Hughes has again produced a short textbook in pediatrics which deserves the highest praise and recommendation. It is obviously intended primarily for medical students and physicians in training, but the quality is of such excellence that it should be well received by physicians across the board. For the modest sum of $10.85 an accurate and up-to-date reference book is available. It would seem an ideal handbook for on-the-spot advice for physicians working in the new comprehensive care programs which often involve the management of sick children outside the hospital setting.

H. E. C. Millar, M.D.

*(Continued on page 34)*

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## Book Reviews

(*Continued from page 33*)

**Disorders of the Respiratory Tract in Children,** by 29 Authorities. Edited by Edwin L. Kendig, Jr., M.D. Price, $26.00. Pp. 834, illustrated. Philadelphia: Saunders, 1967.

This book is a well organized compendium which gives all physicians and surgeons concerned with children a good guide to diagnosis and management of respiratory diseases in the different age groups.

In the first section a modern review of the physiology and biochemistry and, based on this, the pathology of respiration is given with special attention to the newborn. Section 2 introduces practical approaches to diagnosis and therapeutic techniques. Section 3 discusses respiratory diseases in the newborn. The book then touches all the disorders of the respiratory tract, chapter by chapter, from the point of congenital malformations through the various infections, tumors, noninfectious diseases, and other disorders affecting the respiratory tract. This is a good, comprehensive work well illustrated. The X-ray reproductions especially are of fine quality and variety. An extensive bibliography is found at the end of each chapter.

The special value of this book is its emphasis on the constant shifting of disease entities with age. The book could be very helpful to all physicians concerned with children, but due to its extensive nature one can hardly recommend it as a "must" for the busy general practitioner. It should certainly form part of the armamentarium of pediatricians and surgeons working with children.

Agnes E. Schweitzer, M. D.

**Caste and Race: Comparative Approaches.** A Ciba Foundation Volume. Edited by Anthony de Reuck and Julie Knight. Price, $12.00. Pp. 348. Boston: Little, 1967.

This concisely written book is a collection of scholarly reports of a symposium on comparative approaches to the study of caste and race. The symposium, held in London, April 19–21, 1966, was composed of 22 scholarly participants. In addition to front-page matter containing a statement of purpose of Ciba, a list of trustees and officers of the Foundation, preface, table of contents, and a list of members of the symposium, the book has an introduction by the eminent scholar Gunnar Myrdal, who chaired the symposium. Finally, it has an index.

Each of the 11 reports, by a different participant, is followed by a discussion among the 22 total participants of the symposium who are of multinational backgrounds. At the end there is a summary discussion.

Despite the multidisciplinary frames of reference, including anthropology, sociology, social psychology, and social history, the reports hang well together with smooth-flowing continuity of thought. Arranged in chapter fashion, each along with its discussion is numbered in consecutive order. The first part of the book deals with the concepts, history and comparative analysis of caste. It makes specific reference to the caste systems of India and Japan. The middle part contains transitional material through the topic of slavery to the last part, which points up modern ideologies of minority groups and racism. Accordingly, it deals with issues of the European Jew and the American Negro.

This volume makes no value judgments and is almost free of bias. In general, it points out that caste and race have similarities and differences. Moreover, attitudes toward caste vary among different countries and periods as do attitudes toward race. The similarities of caste and race appear in the area of social stratification. The differences are mainly those of purity and impurity for caste as contrasted with economic roots based on skin color for race.

Although the symposium makes a valuable contribution to the study of caste and race, it could perhaps have done better if it had limited its scope of comparison, as suggested in the summary discussion of the book. The book should be read by all students of human behavior.

Luther D. Robinson, M.D.

**Pathology**, 3rd ed. Stanley L. Robbins, M.D. Price, $20.50; 2-volume set, $25.00. Pp. 1434, illustrated. Philadelphia: Saunders, 1967.

This comprehensive text is rapidly becoming a standard in its field. As in the 2 previous editions, most of the material is the work of Dr. Robbins, with contributions by accepted authorities in their specialties. The format is similar to other well known works of pathology, with approximately ⅓ devoted to the principles of general pathology and pathogenetic mechanisms and ⅔ with systemic pathology according to organ systems. The publishers have furnished a quality product with easy-to-read type face and excellent reproductions of photographs, both micro and macro. The subject matter is presented in an easily digestible manner and reflects conflicting points of view where pertinent.

New chapters dealing with genetics and disease, immunological diseases, and pathologic changes of aging have been added in the new edition. Electron photomicrographs are widely used to demonstrate newer discoveries of ultrastructural pathologic changes. The bibliography, a strong point of the previous editions, continues to be excellent and has been updated and thoroughly revised. References are furnished to exhaustive reviews as well as to articles of original research.

While not as encyclopedic as some of the other available general pathology reference texts, this reviewer would rank Robbins' "Pathology" at the top of the list. Medical students, residents, and nonpathologist practicing physicians who wish to keep abreast of current developments in the field of pathology will find this book more than adequate.

Richard L. Levin, M.D.

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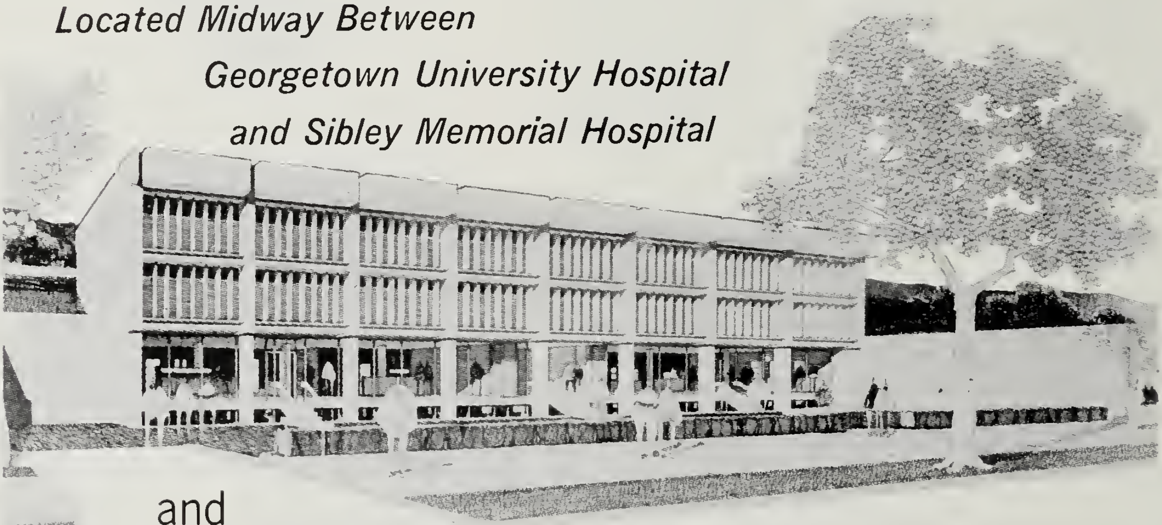

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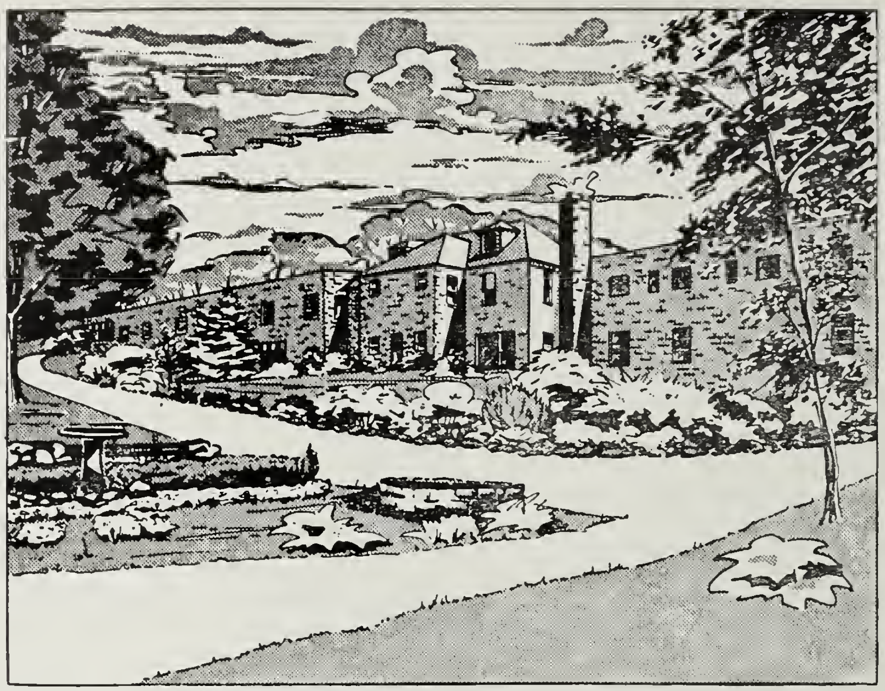

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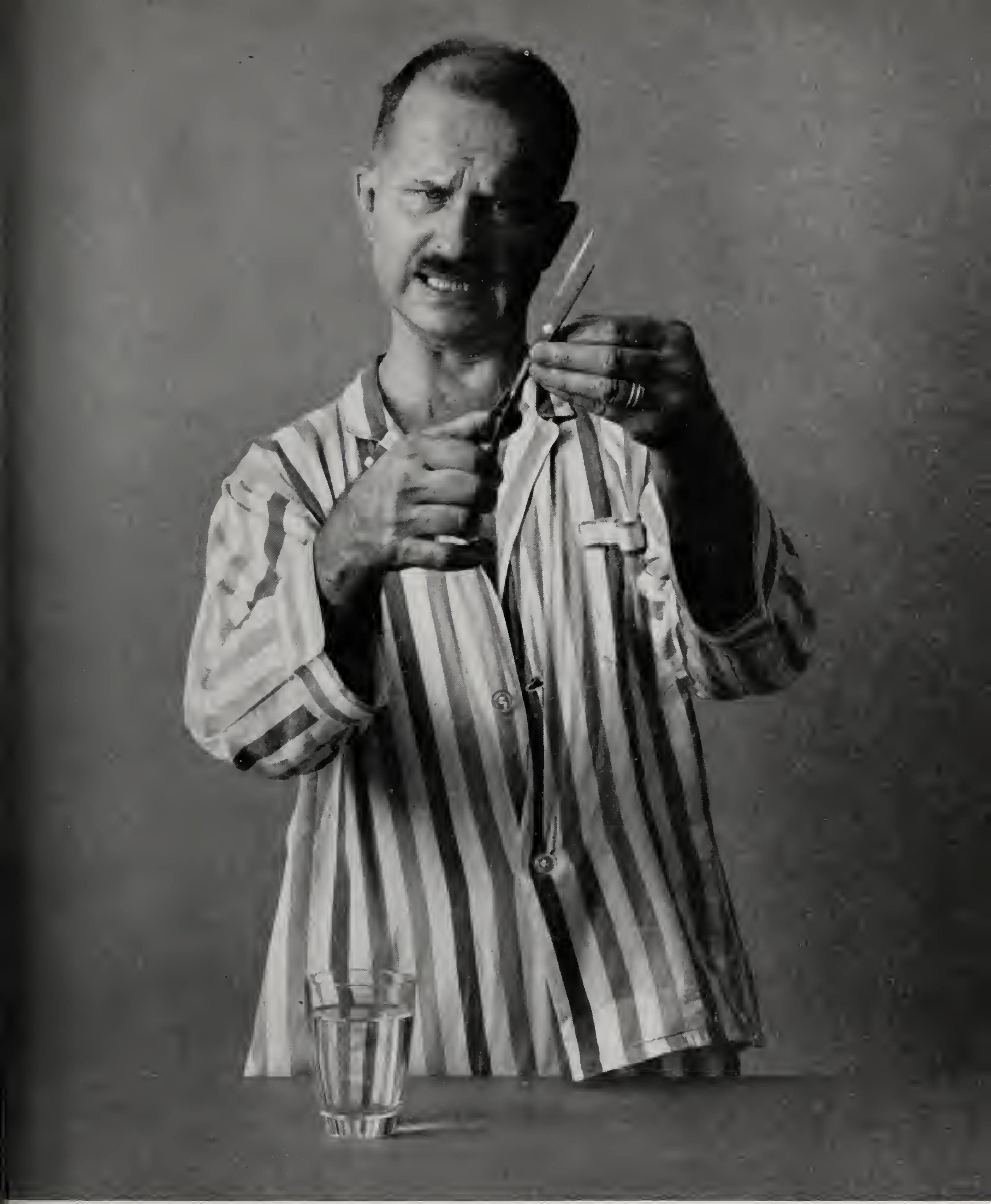

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ted potassium supplements, which should
ised only when adequate dietary supple-
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ll bowel lesions (obstruction, hemor-
ge, and perforation) should be kept in
d. Surgery for these lesions has fre-
ntly been required and deaths have oc-
ed. Discontinue enteric-coated potas-
n supplements immediately if abdominal
, distention, nausea, vomiting, or gastro-
stinal bleeding occur.

with caution in pregnant patients, since
drug may cross the placental barrier and
erse reactions which may occur in the
lt (thrombocytopenia, hyperbilirubinemia,
red carbohydrate metabolism, etc.) are
ential problems in the newborn.

**cautions:** Antihypertensive therapy with
roton should always be initiated cau-
sly in postsympathectomy patients and
atients receiving ganglionic blocking
nts or other potent antihypertensive drugs,
urare. Reduce dosage of concomitant
hypertensive agents by at least one-half.
biturates, narcotics or alcohol may po-
iate hypotension. Because of the possi-
y of progression of renal damage, peri-
: determination of the BUN is indicated.
continue if the BUN rises or liver dysfunc-
is aggravated. Hepatic coma may be
cipitated.

ctrolyte imbalance, sodium and/or potas-
n depletion may occur. If potassium deple-
should occur during therapy, Hygroton
uld be discontinued and potassium sup-
nents given, provided the patient does
have marked oliguria.

e special care in cirrhosis or severe
emic heart disease and in patients re-
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restriction is not recommended.

**erse Reactions:** Nausea, gastric irritation,
iting, anorexia, constipation and cramp-
dizziness, weakness, restlessness, hy-
glycemia, hyperuricemia, headache, mus-
cramps, orthostatic hypotension, aplastic
mia, leukopenia, thrombocytopenia,
anulocytosis, impotence, dysuria, transient
pia, skin rashes, urticaria, purpura, nec-
zing angiitis, acute gout, and pancreatitis
n epigastric pain or unexplained G.I.
ptoms develop after prolonged adminis-
on. Other reactions reported with this
s of compounds include: jaundice, xan-
sia, paresthesia, and photosensitization.

**age Dosage:** One tablet with breakfast
or every other day.

**labiIlty:** White, single-scored tablets of
ng. and aqua tablets of 50 mg., in bot-
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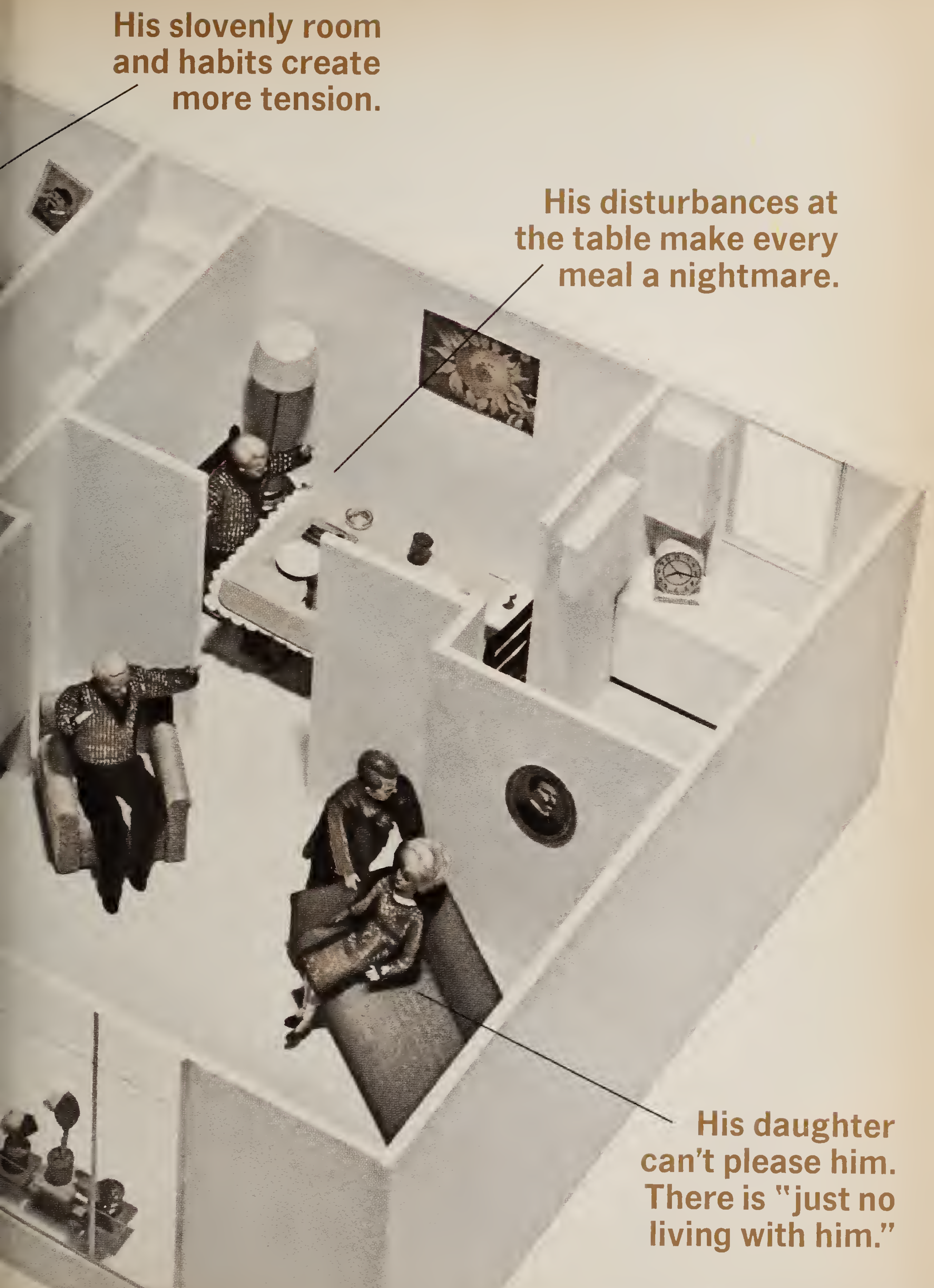
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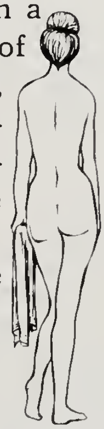

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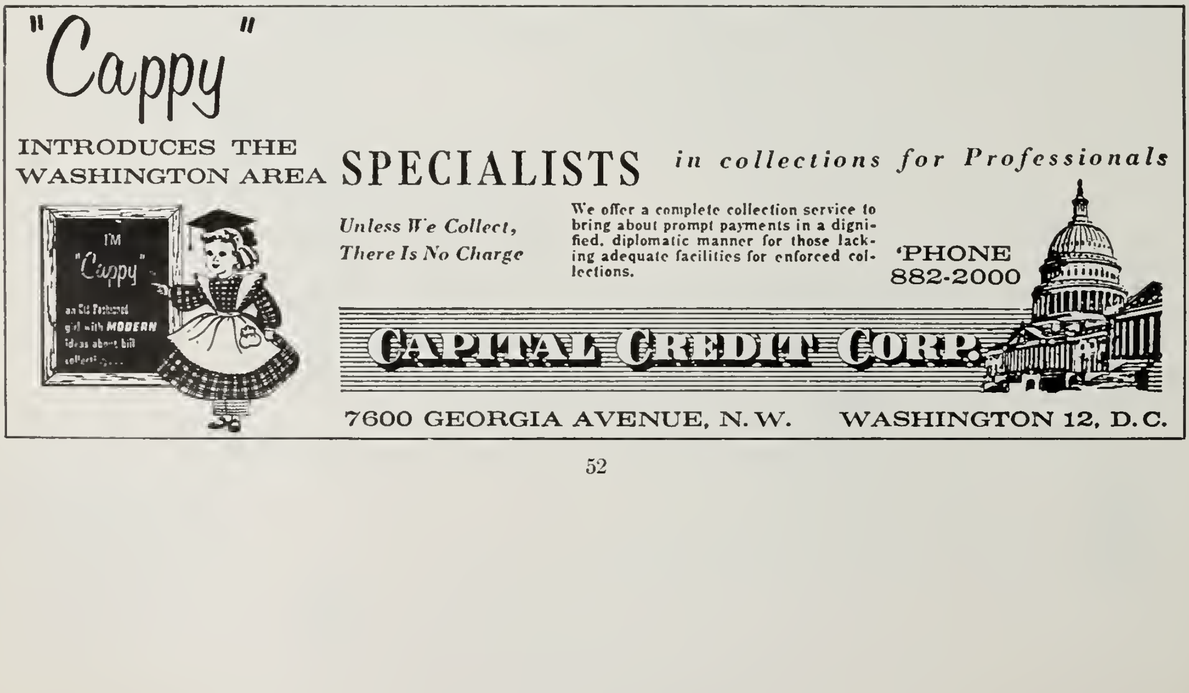
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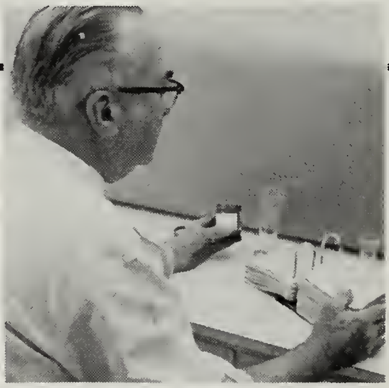
T-text

Count the Prescriptions filled by Peoples Drug Stores and you get 100 million times people have counted on Peoples



We have passed the hundred million mark. That's the number of prescriptions filled by all Peoples Drug Stores since we opened our doors in 1905. We say this with great pride, since this impressive figure illustrates an impressive public confidence. Because behind all prescribed medicine at Peoples is confidence — in the physician who prescribes, the manufacturer who supplies, and the pharmacist who fills the prescription. At Peoples, nothing is more important to us than this confidence.

PEOPLES
PRESCRIPTION DRUG STORES

# A Building Block approach to treating hypertension

ABBOTT

**With these three therapeutic building blocks you can create a once-a-day regimen to fit almost any degree of hypertension. See the following pages for details . . .**

Pargyline Hydrochloride
Deserpidine
Methyclothiazide

# Consider starting your hypertensives on this basic thiazide

ABBOTT

## A single daily dose of Enduron provides sodium excretion around the clock

Enduron is a true 24-hour single-dose thiazide. Its sodium excretion is not squeezed into an abrupt peak during the first several hours. It is well-sustained in a plateau-like effect—with little reduction for the first 12 hours, and decline thereafter only gradual.

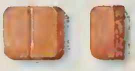
Potassium loss, by contrast, is low. It reaches an early minor peak, then subsides rapidly. Moreover, since dosage is but once a day, there is but one daily peak of potassium loss. As with all thiazides, however, dietary potassium supplementation should also be considered, especially in long or intensive therapy.

Use Enduron as an ideal starting therapy in mild hypertension. Use it too, as a basic therapeutic building block with which other agents can be joined, for managing your more resistant hypertensives.

*Once a day, every day*

**ENDURON®**
METHYCLOTHIAZIDE

ENDURON
ENDURON
METHYCLO-THIAZIDE
2.5 mg
Methyclothiazide

| | Minimum | Usual | Intermediate | Maximum |
|---|---|---|---|---|
| DAILY DOSAGE RANGE | <br>2.5 mg. tablet | <br>5 mg. tablet | <br>7.5 mg. | <br>10 mg. |

*See Brief Summary on final page of advertisement.*

# To build added response, shift to Enduronyl

ABBOTT

## The deserpidine component adds enhanced antihypertensive activity

The rauwolfia component of Enduronyl is deserpidine (Harmonyl®), a purified crystalline alkaloid supplied only by Abbott. It augments Enduron with its own antihypertensive and tranquilizing action.

Thus the combined clinical effect of these two therapeutic building blocks in Enduronyl is greater than can ordinarily be achieved with either alone.

To add flexibility, Enduronyl comes in two strengths: regular and Forte. Both provide 5 mg. of Enduron. The variation is where most helpful: in the deserpidine. The tablets are scored, and give a surprisingly wide and economical choice of once-a-day doses (see below).

Choose Enduronyl for your patients in the broad range of mild to moderate hypertension. Patient acceptance is excellent!

Deserpidine
Methyclothiazide

*Once a day, every day*

**ENDURONYL®**

METHYCLOTHIAZIDE 5 MG. WITH DESERPIDINE 0.25 MG.

**ENDURONYL FORTE**

METHYCLOTHIAZIDE 5 MG. WITH DESERPIDINE 0.5 MG.

| | Minimum | Usual | Intermediate | Maximum |
|---|---|---|---|---|
| DAILY DOSAGE RANGE | <br>2.5 mg. methyclothiazide<br>0.125 mg. deserpidine | <br>5 mg. methyclothiazide<br>0.25 mg. deserpidine | <br>7.5 mg. methyclothiazide<br>0.375 mg. deserpidine | <br>10 mg. methyclothiazide<br>0.5 mg. deserpidine |
| DAILY DOSAGE RANGE | <br>2.5 mg. methyclothiazide<br>0.25 mg. deserpidine | <br>5 mg. methyclothiazide<br>0.5 mg. deserpidine | <br>7.5 mg. methyclothiazide<br>0.75 mg. deserpidine | <br>10 mg. methyclothiazide<br>1 mg. deserpidine |

*See Brief Summary on final page of advertisement.*

707075-R

# Eutonyl affords a different kind of basic therapy for moderate to severe cases

ABBOTT

## Effect tied to reduced peripheral vascular resistance; no central depressant action

Eutonyl is a unique nonhydrazine agent. It is reported to act by reducing peripheral vascular resistance.[1,2]

In clinical trials, significant reductions in mean blood pressure were seen in 84% of patients studied—all were moderate to severe cases. Eutonyl lowers diastolic in proportion to systolic, and in about half of the cases studied, reductions in the sitting and recumbent positions were nearly as great as in the standing position.

Most important: There is no central depressant action. In fact, some patients reported an *increased* sense of well being.

Here, then, is a highly effective *basic treatment* for moderate to severe cases—and one that will not hamper your patient with lethargy or drowsiness while on treatment.

EUTONYL
PARGYLINE HYDRO-CHLORIDE
EUTONYL
25 PARGYLINE HYDRO-CHLORIDE
EUTONYL
50 PARGYLINE HYDRO-CHLORIDE
Pargyline Hydrochloride

*Once a day, every day*

**EUTONYL®**
PARGYLINE HYDROCHLORIDE

| DAILY DOSAGE RANGE | Minimum | Usual starting | Intermediate | Maximum |
|---|---|---|---|---|
| | | | | |
| | 10 mg. tablet | 25 mg. tablet | 50 mg. tablet<br>or as needed | 200 mg. |

---

*1. Brest, A. N., et al., Cardiac and Renal Hemodynamic Response to Pargyline, Ann. N. Y. Acad. Sci., 107-1016, 1963.*
*2. Winsor, T., Pargyline Hydrochloride, Hypertension, Urinary Tryptamine, and Vascular Reflexes, Geriatrics, 19:598, Aug., 1964.*

*See Brief Summary on final page of advertisement.*

# Eutron adds thiazide for enhanced therapy with milder side effects

ABBOTT

**Only a 7/4 mm. span between standing and recumbent pressures in clinical trials—reduced chance of orthostatic hypotension**

The combining of Eutonyl and Enduron in Eutron permits a significantly greater antihypertensive effect than with either agent used alone. This in turn may allow therapeutic success with lesser dosage—and correspondingly milder side effects.

A significant finding in clinical trials was the drug's action in lowering blood pressure to *nearly equal levels in all body positions.* Total average spread between standing and recumbent readings (after treatment) was only 7/4 mm. Hg.

Thus, in your moderate to severe cases, Eutron affords a usually smooth course of therapy, often with reduced likelihood of orthostatic effects. (The usual precautions against rising suddenly, of course, will always apply.) And, because of the thiazide component, Eutron may be used in the presence of congestive heart failure.

EUTRON
Methyclothiazide
Pargyline Hydrochloride

*Once a day, every day*

**EUTRON™**

PARGYLINE HYDROCHLORIDE 25 MG.
WITH METHYCLOTHIAZIDE 5 MG.

| | Minimum | Usual starting | Intermediate | Maximum |
|---|---|---|---|---|
| DAILY DOSAGE RANGE | <br>12.5 mg. pargyline hydrochloride and 2.5 mg. methyclothiazide | <br>25 mg. pargyline hydrochloride and 5 mg. methyclothiazide | <br>37.5 mg. pargyline hydrochloride and 7.5 mg. methyclothiazide | <br>50 mg. pargyline hydrochloride and 10 mg. methyclothiazide |

*See Brief Summary on final page of advertisement.*

TM—Trademark

## ENDURON® | ENDURONYL®

**METHYCLOTHIAZIDE**

Each tablet contains
Methyclothiazide 5 mg. with
Deserpidine 0.25 mg. or 0.5 mg.

*Indications:* Enduron is used to control edema and mild to moderate hypertension; also used with other drugs for hypertension. Enduronyl is used in mild to moderately severe hypertension; when used with Enduronyl, more potent agents can be given at reduced dosage to minimize undesirable side effects.

*Contraindications:* Neither Enduron nor Enduronyl should be used in severe renal disease (except nephrosis) or shutdown; in severe hepatic disease or impending hepatic coma; in patients sensitive to thiazides. Hepatic coma has been reported as a result of hypokalemia in patients receiving thiazides.

Enduronyl is contraindicated in patients with severe mental depression and suicidal tendencies, active peptic ulcer, or ulcerative colitis.

*Warnings:* Consider possible sensitivity reactions in patients with a history of allergy or asthma. If added potassium intake is indicated, dietary supplementation is recommended. Enteric-coated potassium tablets should be reserved for cautious use only when adequate dietary supplementation is not practical because those tablets may induce serious or fatal small bowel lesions consisting of stenosis with or without ulceration. These small bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs.

*Precautions:* Use thiazides with caution in severe renal dysfunction, impaired hepatic function, or progressive liver disease. In surgical patients, thiazides may reduce the response to vasopressors and increase the response to tubocurarine. Use thiazides with caution in pregnancy (bone marrow depression, thrombocytopenia, or altered carbohydrate metabolism have been reported in certain newborn infants). Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. Antihypertensive response may be enhanced following sympathectomy.

Use Enduronyl with caution in patients with a history of peptic ulcer, as rauwolfias may increase gastric secretion. Discontinue at the first sign of mental depression. Rauwolfia alkaloids may increase hypotensive effects of surgery or anesthesia, and should be discontinued two weeks prior. They also lower the convulsive threshold and shorten seizure latency. In epilepsy, dosage adjustment of anticonvulsant medication may be necessary. Alcohol, barbiturates, or narcotics may potentiate action of deserpidine.

*Adverse Reactions:* During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). All patients should be observed for signs of hyponatremia ("low-salt" syndrome). Reported thiazide reactions include: anorexia, nausea, vomiting, diarrhea, headache, skin rash, dizziness, paresthesia, weakness, photosensitivity, jaundice, and pancreatitis.

Reported rauwolfia reactions include: nasal stuffiness, nausea, weight gain, diarrhea, aggravation of peptic ulcer, epistaxis, skin eruption, and reduction of libido and potency. Excessive drowsiness, fatigue, weakness, and nightmares may signal early signs of mental depression.

## EUTONYL® | EUTRON™

**PARGYLINE HYDROCHLORIDE**

Each tablet contains
Pargyline Hydrochloride 25 mg.
with Methyclothiazide 5 mg.

*Indications:* For treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. Not recommended for patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone. It is desirable to establish the dosage of Eutron by administering component drugs separately.

TM-Trademark.

*Contraindications:* Pheochromocytoma, advanced renal disease, increasing renal dysfunction, paranoid schizophrenia and hyperthyroidism. Hepatic coma has been reported as consequence of hypokalemia with thiazide therapy. Until further experience is gained not recommended for patients with malignant hypertension, children under 12, or pregnant patients.

Concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. 2 week interval should separate therapy and use of these agents.

Methyclothiazide is contraindicated in patients with known sensitivity to thiazides.

*Warnings:* Pargyline hydrochloride is a monoamine oxidase inhibitor. Warn patients against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When indicated, alcohol, narcotics (meperidine should be avoided), antihistamines, barbiturates, chloral hydrate, and other hypnotics, sedatives, tranquilizers, or caffeine, may be used cautiously in reduced dosage. In emergency surgery ¼ to ⅕ the usual dose of narcotics, analgesics, and other premedications should be used avoiding parenteral administration where possible. Carefully adjust dose of anesthetics to response of patient. Withdraw pargyline two weeks before elective surgery.

Warn patients about the possibility of postural hypotension. Those with angina or coronary artery disease should not increase physical activity with an improvement in well being. Pargyline may lower blood sugar.

Avoid use of enteric-coated potassium tablets, as these may induce serious or fatal small-bowel lesions consisting of stenosis with or without ulceration. These small-bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs. These products contain no added potassium salts and if added potassium intake is desired, dietary supplementation is recommended. Coated potassium tablets should be reserved for cautious use when adequate dietary supplementation is impractical. In patients with a history of allergy or asthma the possibility of sensitivity reactions should be considered.

*Precautions:* Measure blood pressure while patient is standing to determine antihypertensive effect. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Use with caution in patients with liver disease. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. With prolonged therapy, examine patients for change in color perception, visual fields and fundi. Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. In surgical patients thiazides may reduce response to vasopressors and increase response to tubocurarine.

*Adverse Reactions:* Pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extrapyramidal symptoms have been reported in a few patients with reduced cardiac reserve.

During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). Observe all patients for signs of hyponatremia ("low salt" syndrome).

Reported thiazide reactions also include anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, and pancreatitis. Nocturia has been observed with the combination.

709075R

ABBOTT

MEMO FROM . . .

to :

DR. "A"*
Administrator, Income Protection Plan,
Medical Society of the District of Columbia

***"Thank you for relieving me of a financial burden"***

Dr. "A", Washington, D.C., was mighty thankful he had the Medical Society's Income Protection Plan when he was disabled recently by an accident.
Mutual of Omaha, underwriter of the plan, sent Dr. "A" a check for $2,562.60, paying him benefits under his Medical Society coverage as well as the supplementary coverage he has had with Mutual of Omaha since 1932.

All told, Mutual of Omaha has paid Dr. "A" a total of $8,003.38 in benefits since 1955. These checks, covering three separate disabilities, have helped him meet his financial obligations when he was unable to carry on his practice.
On each occasion Dr. "A" has been completely satisfied with the manner in which his applications for benefits have been handled and said so in a recent letter to Mutual of Omaha.
To put it in his own words: "I feel that my best friend in time of need has been Mutual of Omaha."

Others Sing the Praises of Their Medical Society Protection Too:

Dr. "B"*
Laurel, Maryland

Since purchasing his Medical Society Income Protection Plan in 1953, Dr. "B" has been disabled five times. He has received benefit checks totaling $1,199.91. Says Dr. "B": "I can truly state that I am very satisfied with my policy with Mutual of Omaha and wish to express my sincere thanks."

Dr. "C"*
Washington, D. C.

When Dr. "C" received his benefit draft for $1,050.00 he commented that he was "most gratified to hear from Mutual of Omaha. Payment of sick benefits was made promptly, and was most appreciated at that time. I have nothing but praise for your organization and appreciate very much the privilege of holding a policy with you."

Dr. "D"*
Glenn Dale, Maryland

After receiving benefits five times for a total of $628.54, Dr. "D" has this to say about his Mutual of Omaha coverage: "I would not hesitate to recommend your company to any of my friends, and can understand why Mutual of Omaha was selected to underwrite the Medical Society's group plan."

These people know from experience the importance of protecting their most valuable asset—*their ability to earn an income*. How about you? Is your income protected? If not, contact your Medical Society's Insurance Administrator today. He'll be happy to give you full details on the Medical Society's own Income Protection Plan, the same outstanding coverage that has provided so much financial security to these, your fellow members, in time of sickness or accident. It's the only plan specifically designed for Medical Society members by Mutual of Omaha, the greatest name in health insurance.

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**5-mg, 10-mg, 25-mg tablets**

ROCHE

Before prescribing, please consult complete product information, a summary of which follows:

**Contraindications:** Patients with known hypersensitivity to the drug.

**Warnings:** Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of child-bearing age requires that its potential benefits be weighed against its possible hazards.

**Precautions:** In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.,* excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

**Adverse Reactions:** Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver-function tests advisable during protracted therapy.

**Usual Daily Dosage:** Individualize for maximum beneficial effects. *Oral*—Adults: Mild and moderate anxiety and tension, 5 or 10 mg t.i.d. or q.i.d.; severe states, 20 or 25 mg t.i.d. or q.i.d. Geriatric patients: 5 mg b.i.d. to q.i.d. (See Precautions.)

**Supplied:** Librium® (chlordiazepoxide HCl) Capsules, 5 mg, 10 mg and 25 mg—bottles of 50. Libritabs^T.M.^ (chlordiazepoxide) Tablets, 5 mg, 10 mg and 25 mg—bottles of 100. With respect to clinical activity, capsules and tablets are indistinguishable.

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Merry Christmas
•
Happy New Year

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PRECAUTIONS: Periodic examination of the blood is advisable. Nystagmus in combination with diplopia and ataxia indicates dosage should be reduced. The possibility of toxic effects during pregnancy has not been explored. ADVERSE REACTIONS: Allergic phenomena such as polyarthropathy, fever, skin eruptions, and acute generalized morbilliform eruptions with or without fever. Rarely, dermatitis goes on to exfoliation with hepatitis, and further dosage is contraindicated. Gingival hypertrophy, hirsutism, and excessive motor activity are occasionally encountered. During initial treatment, side effects may include gastric distress, nausea, weight loss, nervousness, sleeplessness, feeling of unsteadiness. Macrocytosis, megaloblastic anemia, leukopenia, granulocytopenia, thrombocytopenia, pancytopenia, agranulocytosis, and aplastic anemia have been reported. Nystagmus, lymphadenopathy, lupus erythematosus, erythema multiforme (Stevens-Johnson syndrome), and a syndrome resembling infectious mononucleosis with jaundice have occurred.
DILANTIN is supplied in several forms including Kapseals® containing 0.1 Gm. and 0.03 Gm. diphenylhydantoin sodium.
Parke, Davis & Company, Detroit, Michigan 48232

The color combinations of the banded capsules are Parke-Davis trademarks. The orange-banded white capsule identifies Parke-Davis 0.1 Gm. diphenylhydantoin sodium; the pink-banded white capsule 0.03 Gm. diphenylhydantoin sodium.

**PARKE-DAVIS** 015R67

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- Literature on indications and dosage available on request.
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- Supplied in bottles of twenty-five 3,000 unit tablets.

(In vivo measurement of Lutrexin on contracting uterine muscle of the guinea pig.)

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# MEDICAL ANNALS

*of the District of Columbia*

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Relief of hyperacidity is still a primary goal in the treatment of peptic ulcer. And antacids are the most widely used means of achieving this relief. But antacids alone cannot influence the distention and bloating which so often add to ulcer distress.

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*the two most widely used antacids*—magnesium and aluminum hydroxides—to help secure rapid acid neutralization with little chance of laxation or constipation;

**PLUS**

*the defoaming action of simethicone*—to help relieve the painful gas symptoms which often accompany peptic ulcer.

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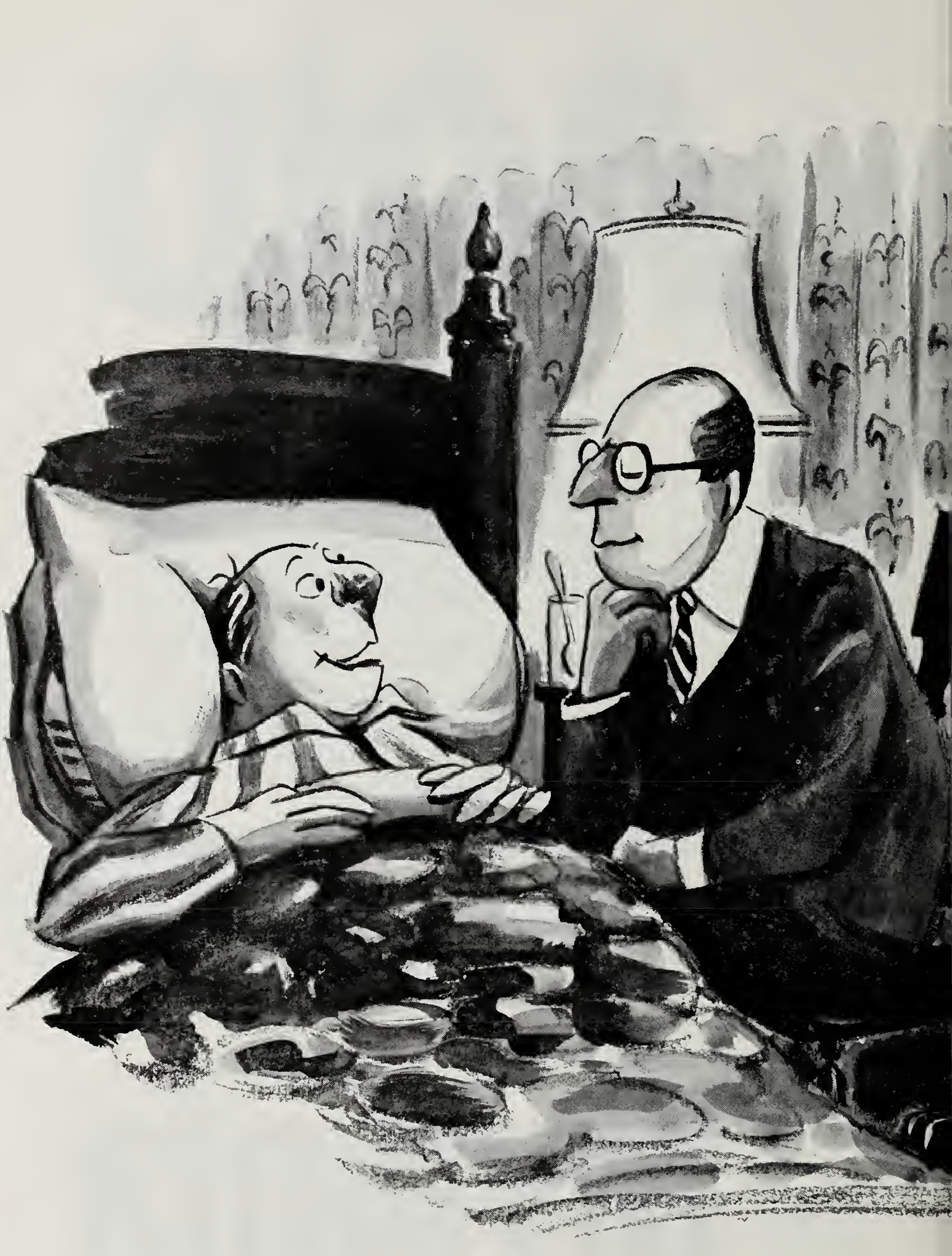
antacid therapy plus an added benefit

nonfatiguing flavor/smooth pleasant texture; both assure patient cooperation during long-term therapy.

Stuart Division of / ATLAS CHEMICAL INDUSTRIES, INC. / Pasadena, Calif.



*"When I couldn't even smell corned beef and cabbage, I decided it was time for you, Doc."*

Maybe he doesn't know when he's well off. But you might want to prescribe long-acting Novahistine LP anyway.

Two tablets in the morning and two in the evening will usually provide day and night relief by helping to clear congested air passages for normal, free breathing. Novahistine LP is formulated to provide continuous therapeutic effect for 8 to 12 hours. The decongestant ingredients help restore normal mucus secretion and ciliary activity—physiologic defenses against infection of the respiratory tract. Use cautiously in individuals with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Caution ambulatory patients that drowsiness may result. Each Novahistine LP tablet contains phenylephrine hydrochloride, 25 mg., and chlorpheniramine maleate, 4 mg.

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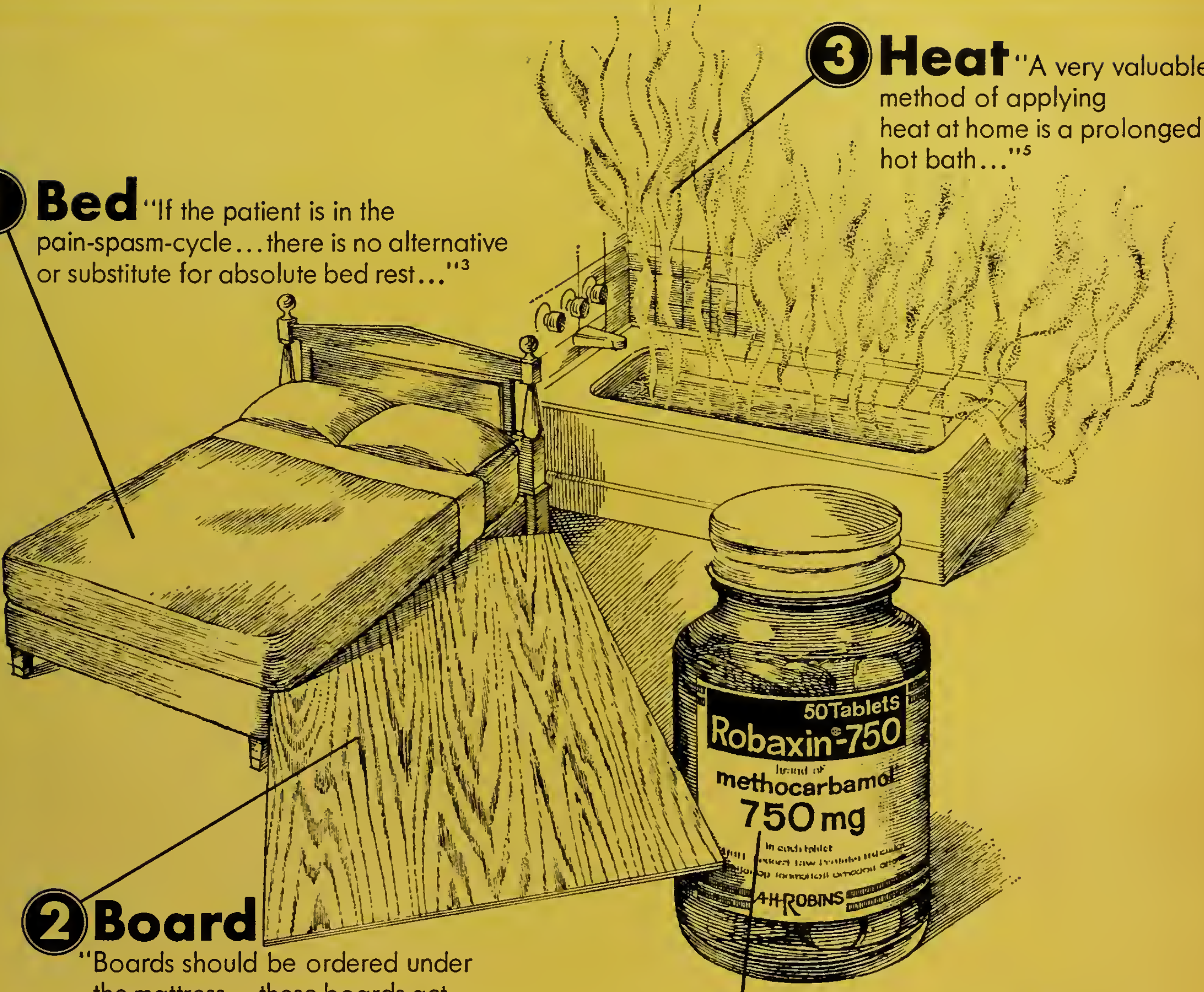
# LOW-BACK PAIN

## A CONSERVATIVE, FOUR-POINT PROGRAM

**The low back pain that is most frequently seen in general practice is mechanical in nature, i.e., postural back pain, joint dysfunction and acute back strain.[1,2] For this type of discomfort, a conservative regimen is usually sufficient to relieve aches and pains, and to help keep the patient functioning. Components of this basic program include:**



③ **Heat** "A very valuable method of applying heat at home is a prolonged hot bath..."[5]

① **Bed** "If the patient is in the pain-spasm-cycle...there is no alternative or substitute for absolute bed rest..."[3]

② **Board** "Boards should be ordered under the mattress...these boards act by immobilizing the spine..."[4]

④ **Robaxin®-750** (methocarbamol, 750 mg. capsule-shaped tablets) A well-tolerated[6] skeletal muscle relaxant, methocarbamol helps relieve spasm "...without interfering with normal tone and movement."[7] And there is little likelihood of sedation.[6]

**Indicated** for relief of skeletal muscle spasm. **Contraindicated** in hypersensitive patients. **Side Effects** (lightheadedness, dizziness, drowsiness, nausea) may occur rarely, but usually disappear on reduced dosage. Hypersensitivity reactions develop infrequently. See product literature for further details. **Also available:** Robaxin® Tablets (methocarbamol, 500 mg.) Robaxin Injectable (methocarbamol, 1 Gm./10 cc.)

**References:** (1). Godfrey, C.M.: Applied Therap. 8:950, 1966. (2). Gottschalk, L.A.: GP 33:91, 1966. (3). Rowe, M.L.: J. Occup. Med. 2:219, 1960. (4). Cozen, L.: South Dakota J. Med. 18:26, 1965. (5). Soto-Hall, R.: Med. Sc. 14:23, 1963. (6). Weiss, M. and Weiss, S.: J. Am. Osteopath. A. 62:142, 1962. (7). Feuer, S.G., *et al.*: New York J. Med. 62:1985, 1962.

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Each tablet contains: Codeine Phosphate gr. ½ (Warning—May be habit forming), Phenacetin gr. 2½, Aspirin gr. 3½, Caffeine gr. ½.

■ Despite introduction of synthetic substitutes, efficacy of 'Empirin' Compound with Codeine remains unchallenged.

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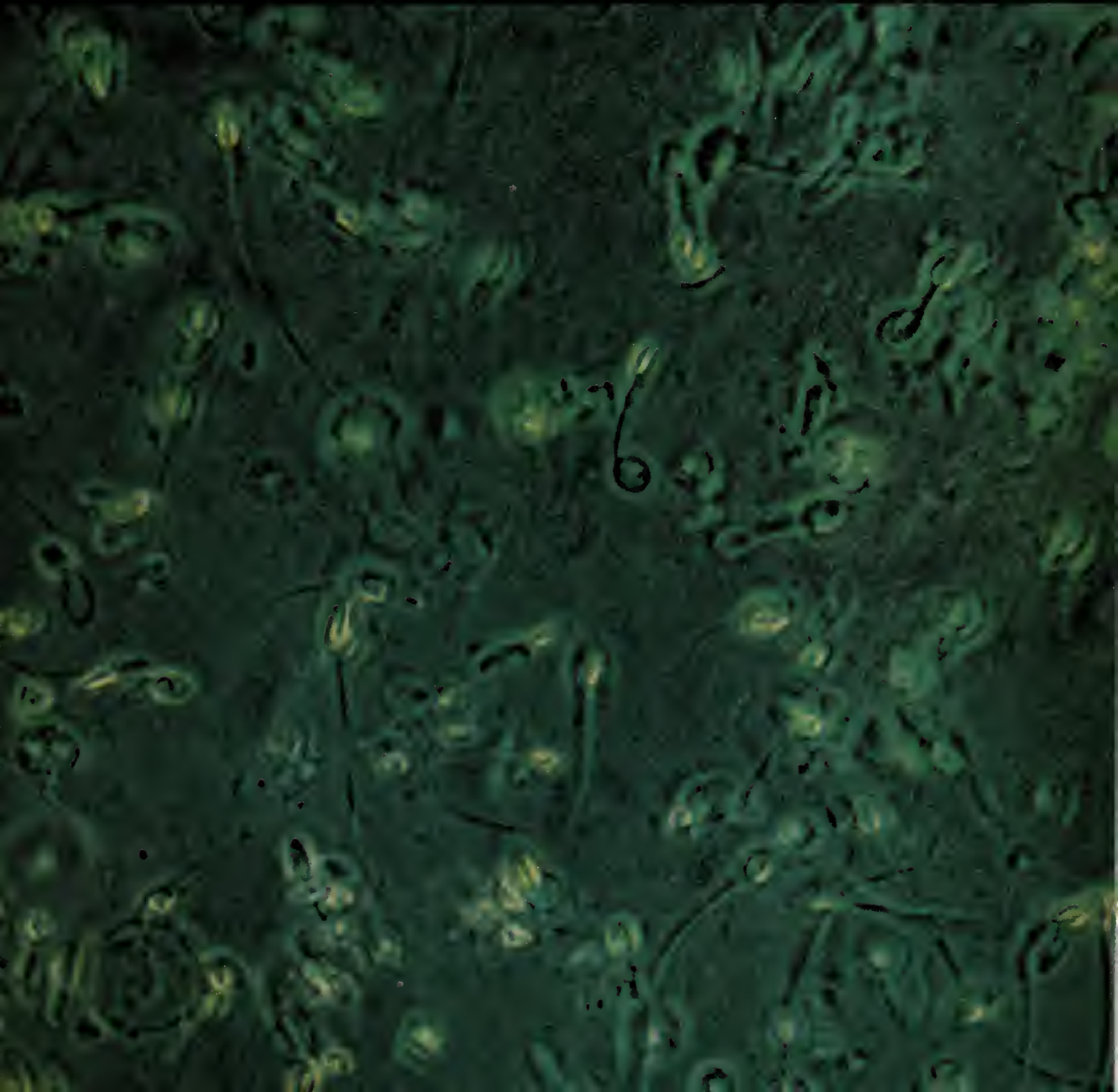
When the talk turns to oral contraceptives, it makes medical sense to remember low-dose Norinyl®-1.

(norethindrone 1mg. c̄ mestranol 0.05mg.)

Turn page for contraindications, precautions and side effects.



Reduction of oral contraceptive dosage to the lowest effective levels is a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now also available as Norinyl-1, containing exactly one half the previous dosage of norethindrone and mestranol. Clinical experience has established that effective fertility control can be achieved with the same degree of reliability and safety with new Norinyl-1 when taken as directed.

What about switching patients from higher dosage forms?

In transferring patients to low-dose Norinyl-1 from higher-dosage oral contraceptives, some breakthrough bleeding may occur in the early cycles. In the majority of cases the bleeding episode is mild and self-limited. The long-term advantages of the lower dosage form should be weighed against the inconvenience of possible breakthrough bleeding in the individual patient.

*Prescribing Information*

*Contraindications:* Patients with any symptoms or history of thrombophlebitis, pulmonary embolism, liver dysfunction or disease, carcinoma of breast or genital organs, or undiagnosed vaginal bleeding.

*Warnings:* Discontinue medication pending examination if there is sudden partial or complete loss of vision, proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. The safety of Norinyl-1 in pregnancy has not been demonstrated. If a patient misses two consecutive periods, pregnancy should be ruled out before continuing the medication. If she has not adhered to the prescribed schedule, pregnancy should be considered at the first missed period. Active ingredients of oral contraceptives have been detected in the milk of mothers who received these drugs; the significance to infants has not been determined.

*Precautions:* Pretreatment physical should include examination of the breasts and pelvic organs, as well as a Papanicolaou smear. If endocrine or liver function tests are abnormal during therapy, repeat tests are recommended after the drug has been withdrawn for two months. Following administration of drug, preexisting uterine fibromyomata may increase in size. Careful observation and caution are required for patients with symptoms or history of epilepsy, migraine, asthma, cardiac or renal dysfunction, cerebrovascular accident, psychic depression, and diabetes. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. Possible long-term effects of the drug on pituitary, ovarian, adrenal, hepatic or uterine function must await further studies. The physician should be alert to the earliest manifestations of thrombophlebitis and pulmonary embolism. The drug should be used judiciously in those young patients in whom bone growth is not complete. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask symptoms of the climacteric. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

*Side Effects:* The following have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals, mental depression. Although the following side effects have been reported in users of oral contraceptives, no cause and effect relationship has been established: anovulation posttreatment, premenstruallike syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, and itching. The following occurrences have been observed in users of oral contraceptives (a cause and effect relationship has neither been established nor disproved): thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory tests may be altered by the use of oral contraceptives: increased sulfobromophthalein and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in $T^3$ values), metyrapone test, pregnanediol determination.

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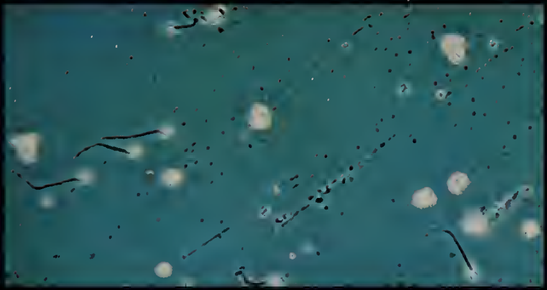
# Here's why Norinyl-1 makes medical sense.

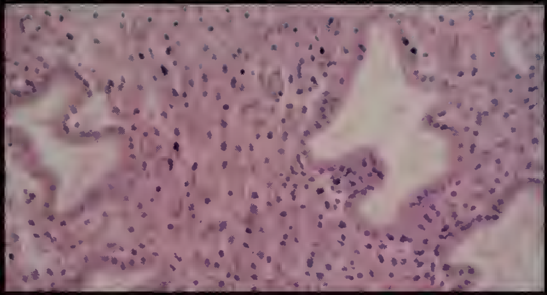
The effectiveness of Norinyl-1 as a low-dose oral contraceptive may be explained by its possible multiple action. In addition to its primary action of suppression of ovulation, Norinyl-1 may offer additional protective mechanisms . . . (1) creation of a cervical mucus that may be hostile to sperm penetration, and (2) development of an endometrium that may be out of phase with nidation. These effects are illustrated below.

**Untreated Patient**

Cervical mucus at midcycle is usually thin and watery, with Spinnbarkeit (stretchability) of 15 to 20 cm.



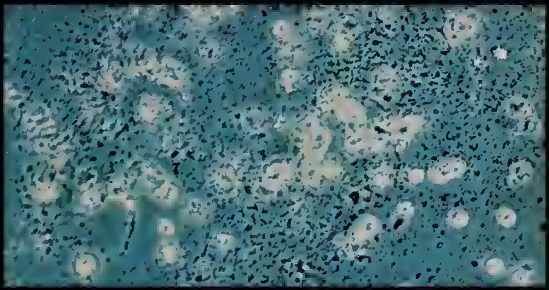
Spermatozoa appear healthy, active, freemoving.



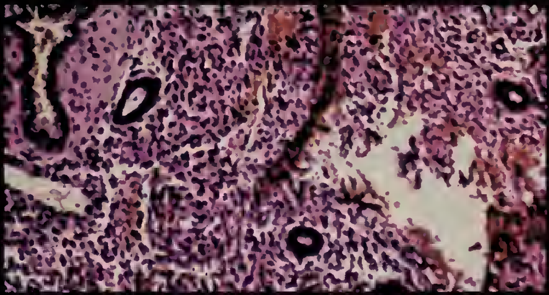
Endometrium of untreated patient is receptive to the fertilized ovum during secretory phase.

**Norinyl-1 Patient**

Cervical mucus at midcycle is scanty, viscous—with Spinnbarkeit of 1 cm. or less.



Immobile spermatozoa as they appear in cervical mucus taken from patient treated with Norinyl-1.



Norethindrone in Norinyl-1 accelerates secretory phase, suppresses glandular and vascular development.

**Norinyl®-1 tablets**
(norethindrone 1mg. c̄ mestranol 0.05mg.)

- new low dose of time-proved ingredients
- established norethindrone/mestranol ratio
- lower patient cost

# An uncommon steroid for common inflammatory dermatoses

In everyday topical steroid therapy, Synalar produces rapid resolution of inflammation and itching in steroid-responsive dermatoses—and at relatively low cost to the patient.

**Advanced molecular design enhances potency**

Synalar combines the advantage of earlier corticosteroid compounds with unique structural innovations. As a result, preparations of Synalar 0.01% and Synalar 0.025% have been reported to be more potent topically and significantly more effective than hydrocortisone 1.0%. The unique fluocinolone acetonide molecule provides one of the most useful topical corticosteroids for everyday practice.

**Impressive clinical results in a wide range of dermatologic problems**

The clinical efficacy of Synalar has been extensively documented in the world literature. Commonly encountered diseases such as allergic and contact dermatitis, eczematous and seborrheic dermatitis, and neurodermatitis respond rapidly to Synalar, often where previous therapy with other topical corticosteroids has failed.

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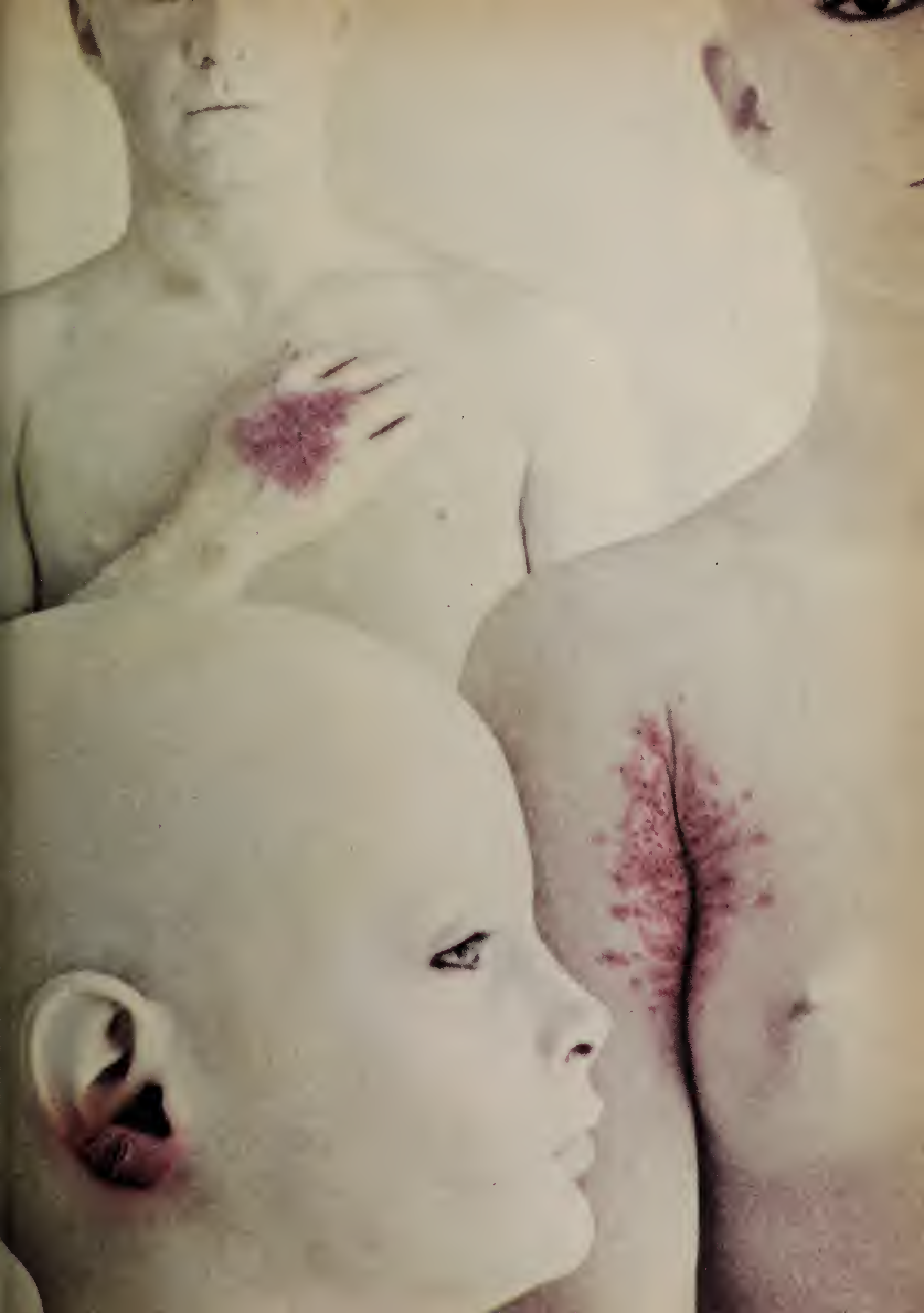
With Synalar, a high degree of efficacy does not mean high price. And—a small quantity goes a long way. Thus, your patients can often obtain the "economy" of a hydrocortisone preparation with the proved efficacy of a potent, truly advanced steroid.

**Synalar®**
fluocinolone acetonide



# For everyday topical steroid therapy
# **Synalar® 0.01%**
## fluocinolone acetonide
## provides economy in two practical dosage forms

For general use, the most economical and widely applicable concentration of Synalar is 0.01% Cream in a water-washable, vanishing cream base. Synalar Solution 0.01% is especially valuable in dermatoses involving moist, intertriginous areas or hairy sites where creams and ointments do not spread or penetrate readily. Synalar Solution is a unique dosage form—clear, nongreasy, cosmetically elegant.

*Product Information*

*Contraindications:* Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. *Precautions:* Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. *Side Effects:* Side effects are uncommon with topical corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. In such cases the agent should be discontinued and appropriate measures taken. *Availability:* Synalar (fluocinolone acetonide) Cream 0.025%—5, 15 and 60 Gm. tubes and 425 Gm. jars. Cream 0.01%—15, 45 and 60 Gm. tubes and 120 Gm. jars. Solution 0.01%—20 and 60 cc. plastic squeeze bottles. Ointment 0.025%—15 and 60 Gm. tubes. Neo-Synalar® (neomycin sulfate 0.5% [0.35% neomycin base], fluocinolone acetonide 0.025%) Cream—5, 15 and 60 Gm. tubes.

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# BOOK REVIEWS

**Diabetes Mellitus: Diagnosis and Treatment.** Volume II. Prepared under the auspices of the Committee on Professional Education of the American Diabetes Association, Inc. GEORGE J. HAMWI, M.D., AND T. S. DANOWSKI, M.D., Editors. Price, $2.50. Pp. 250. New York: American Diabetes Association, 1967.

In 1964 the American Diabetes Association issued the first volume of this publication in an effort to provide practical, concise, and up-to-date information for the physician. This second volume is "not meant to replace, but rather to supplement the first volume."

The 41 articles in Volume II were written by 47 nationally known authors whose major interest is in the research, diagnosis and treatment of diabetes mellitus. New subjects discussed include physical activity and diabetic control, nonketo-acidotic coma, hypophysectomy in diabetic retinopathy, special problems associated with diabetic infants and children, and the socioeconomic problems associated with the disease. Subjects such as pregnancy and diabetes and the various vascular complications which were also included in Volume I have been discussed by authors who did not appear in the previous publication, thus bringing a different approach and updating the subject matter.

Physicians desiring to have available a compact source of present-day knowledge concerning the diagnosis and treatment of diabetes will do well to own this book.

E. CLARENCE RICE, M.D.

**Manual of Preoperative and Postoperative Care** by the Committee on Pre- and Postoperative Care, American College of Surgeons. Editorial Subcommittee: HENRY T. RANDALL, M.D., Chairman; JAMES D. HARDY, M.D., AND FRANCIS D. MOORE, M.D. Price, $8.50. Pp. 506. Philadelphia: Saunders, 1967.

This manual is essentially divided into 2 parts, the first dealing with the general problems that one may experience in the pre- and postoperative periods as they apply to fluid and electrolytic therapy, metabolic problems, nutrition, hemodynamic stability, sepsis, burns, etc. These topics are applied to the organ systems, especially the cardiovascular, gastrointestinal, respiratory, and urological ones. Some chapters border on the esoteric, i.e., Metabolic Problems of Surgical Patients, but all are easily comprehended. The chapters on Evaluation and Management of Ventilation and the one on Diagnosis and Management of Acute Renal Failure I thought were of special merit. Others reading this manual will find other chapters equally noteworthy.

The second portion of the manual discusses the special problems that one may encounter in the pre-, intra- and postoperative periods in specific organ systems. Because many of these problems include electrolyte and fluid balance, hemorrhage, sepsis, etc., an unavoidable overlap exists with most of the repetition noted in the introduction of each chapter. The more recent advances in each organ system, especially as regards treatment, are discussed.

In general, the manual provides a concise outline of subject matter so necessary to the practicing surgeon. Easily read and well organized, it makes for an ideal reference tool for the busy surgeon when encountering a difficult problem in management. Since it intends to be no more than an outline, an excellent bibliography appears at the end of each chapter.

MARTIN H. EICHLER, M.D.

**Ciba Foundation Symposium: Development of the Lung.** Edited by A. V. S. DE REUCK, M.Sc., D.I.C., A.R.C.S., AND RUTH PORTER, M.R.C.P. Price, $13.00. Pp. 408, with 134 illustrations. Boston: Little, 1967.

This symposium deals with 5 areas of physiological and physiochemical research into the functional development of the lung in man and animals. Many prominent authorities from around the world have contributed to the symposium. Each of 19 papers is discussed by a panel of experts with a great deal of information contributed to each discussion by workers in allied and nonallied areas.

Phylogeny of the lung is discussed in the first section. The papers by H. Rahn and J. Kylstra on respiration by liquid-filled lungs are provocative for their possible space age applications. The second section on ontogeny examines the embryology of the lung and leads into the thorough discussion of alveolar function at the gas/liquid interface by John A. Clements. The effect of temperature change on alveolar function is explored, and some clinical implication may be made for hypothermic states during cardiac surgery.

Section 3 is a discussion of intra-uterine gas exchange with a comparison of this function in several species. The start of breathing is explored in the fourth section followed by a group discussion on several pertinent topics presented in the papers. New ideas are expressed along with misgivings about old concepts.

This is a book for the pulmonary physiologist but not for the clinician as claimed. The technical jargon will cause most nonphysiologists to lose interest, and most areas discussed require a great deal of refinement before clinical applications can be made.

The Ciba Foundation is commended for bringing together such a fine group and producing a comprehensive symposium on structural, physiological, and physiochemical development of the lung.

JAMES D. SHEPPERD, JR., M.D.

**Atlas of Intestinal Stomas.** RUPERT B. TURNBULL, JR., M.D , F.A.C.S., AND FRANK L. WEAKLEY, M.D. Price, $21.50. Pp. 207, with 182 illustrations by Robert M. Reed. St. Louis: Mosby, 1967.

The Atlas reflects the evolution of ileostomy and colostomy in the United States and England.

The discovery by Richard Warren and Leland McKittrick in 1951 that the greatly feared syndrome of watery discharge, abdominal cramps, vomiting and hypovolemia in ileostomy patients represented stomal obstruction led to these technical investigations.

*(Continued on page 22)*

## Diagnosis:

**cystitis?**
**pyelonephritis?**
**pyelitis?**
**urethritis?**
**prostatitis?**

in any case,
usually gram-negative*

## Therapy:

two 500 mg. Caplets® q.i.d.
(initial adult dose)

# NegGram®

Brand of
**nalidixic acid**

a specific anti-gram-negative

eradicates most urinary tract infections...

- Low incidence of untoward effects; no fungal overgrowth, crystalluria, ototoxic or nephrotoxic effects have been observed.

- "Excellent" or "good" response reported *in more than 2 out of 3* patients with either chronic or acute gram-negative infections.[1]

*As many as 9 out of 10 urinary tract infections are now caused by gram-negative organisms: E. coli, Klebsiella, Aerobacter, Proteus, Paracolon or Pseudomonas[2]... However, infections of the urethra and prostate caused by non-gonococcal gram-negative organisms are believed to be less prevalent.

**ummary of prescribing information**

**ıdications:** Urinary tract infections in which gram-negative bacteria are pre-ominant, particularly *Proteus, Escherichia coli, Aerobacter, Klebsiella,* and ertain strains of *Pseudomonas*. Gram-positive bacteria are less sensitive to egGram but favorable clinical results have been observed.

**/arning:** Use in Pregnancy. This drug is not recommended in the first tri-ıester of pregnancy. However, it has been used in several patients during ıe last two trimesters without producing apparent ill effects in either mother r fetus.

**recautions:** As with all new drugs, periodic blood and liver function tests re advisable during treatment longer than 1 or 2 weeks. **This drug should be sed with caution in patients with liver disease, epilepsy, severe cerebral rteriosclerosis, or severe impairment of kidney function.** Because photo-ensitivity reactions have been reported in a small number of cases, patients ıould be cautioned to avoid unnecessary exposure to direct sunlight while eceiving NegGram, and if a photosensitivity reaction occurs, therapy should e discontinued. The dosage recommended for adults and children should not rbitrarily be doubled unless under the careful supervision of a physician. hould bacterial resistance develop or additional nonsensitive strains emerge, ther effective antibacterial agents should be added to or substituted for egGram.

/hen testing the urine for glucose in patients receiving NegGram, Clinistix® eagent Strips or Tes-Tape® should be used since other reagents may give false-positive reaction.

**dverse reactions:** Mainly mild nausea, vomiting, and other gastrointestinal sturbances; less frequently, sleepiness, drowsiness, weakness, headache, izziness and vertigo, and rarely cholestasis, paresthesia, thrombocytopenia, ukopenia, or hemolytic anemia in patients with a deficiency in activity of ucose-6-phosphate dehydrogenase. Itching, pruritus, rash, urticaria, mild osinophilia, reversible photosensitivity reactions primarily involving exposed ırfaces, and reversible subjective visual disturbances (overbrightness of lights, ıange in visual color perception, difficulty in focusing, decrease in visual acuity ıd double vision), occurred occasionally. Reversible increased intracranial essure with bulging anterior fontanel, papilledema, and headache has been oserved occasionally in infants and children. Toxic psychosis and brief con-ılsions (the latter generally in patients with possible predisposing factors, ıd both usually associated with excessive dosage) have been recorded in re instances.

**osage and administration:** ***Adults*—Four Gm. daily by mouth (2 Caplets® of 0 mg. four times daily) for one to two weeks. Thereafter, if prolonged eatment is indicated, the dosage may be reduced to two Gm. daily (1 Caplet 500 mg. four times daily). *Children*—According to age and weight: approxi-ately *25 mg. per pound* of body weight per day, administered in divided doses.**

**ote: The dosage recommended above for adults and children should not arbi-arily be doubled unless under the careful supervision of a physician. Until rther experience is gained, infants under 1 month should not be treated with e drug.**

**ow supplied:**

**For adults**—Buff-colored, scored Caplets of **500 mg.**, conveniently available bottles of 56 (sufficient for one full week of therapy) and in bottles of 1000.

**For children**—Caplets of **250 mg.**, available in bottles of 56 and 1000.

**efore prescribing, please refer to complete prescribing information.**

**eferences:** (1) Based on 23 clinical papers, 1512 cases. Bibliography on re-ıest. (2) Bush, I. M., Orkin, L. A., and Winter, J. W., in Sylvester, J. C.: ıtimicrobial Agents and Chemotherapy—1964, Ann Arbor, American Society r Microbiology, 1965, p. 722.

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## Book Reviews

(*Continued from page 20*)

The 182 illustrations could serve as an indispensable aid to the young surgeon in preventing this tragedy and bringing new hope to the internist and patient. Technical details of stomal size, site, and primary eversion to prevent stomal obstruction and prolapse are presented.

Poorly constructed stomas can be corrected by such innovations as mucosal grafted ileostomy, logitudinal slitting of seromuscular layers, transplantation, skin grafting, and shortening of the ileostomy.

Special considerations, such as ileostomy in obesity, are depicted with great clarity.

Illustrations of safe techniques in the construction and immediate opening of colostomies for decompression as well as fecal diversion complete an Atlas long awaited by the surgical world.

Edward G. Fisher, M.D.

**Ciba Foundation Study Group No. 28: Thiamine Deficiency: Biochemical Lesions and Their Clinical Significance.** Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Maeve O'Connor, B.A. Price, $4.50. Pp. 163, with 46 illustrations. Boston: Little, 1967.

This small volume represents the Ciba Foundation Study Group No. 28 which met in November, 1966. A number of distinguished physiologists took part in the discussions, which were dedicated to Sir Rudolph Peters. Dr. Peters opened the session with an historical review of the early work in animals which led to the first demonstration of one of the actions of thiamine in vitro. The ability of thiamine to increase oxygen uptake in brain brei was the first observation of the action of any vitamin in vitro.

The other papers contained in this book deal with such topics as the value of pyruvate determination in thiamine deficiency, enzyme defects in thiamine deficiency, and the role or lack of role played by thiamine in the neurological lesion seen in beriberi. This reviewer was impressed by the somewhat historical nature of each of the presentations. Much of the material obviously had been printed 3 or more years earlier, and the discussions following each paper, while focusing on basic areas of divergence, did not do more than rehash arguments that have probably been discussed at international meetings over the past 10 years.

It seems that this book would be of value to someone new to the field. It is of little clinical value except for the references, since, as is pointed out several times, animal and human thiamine deficiencies are quite distinct clinically and biochemically.

The one stated object was to decide if more than one biochemical lesion exists in thiamine deficiency. That question was not answered, but it was approached.

Jay R. Shapiro, M.D.

## NATIONAL AND REGIONAL MEETINGS

December 26–31: American Association for the Advancement of Science. New York. Address: Dr. R. L. Taylor, 1515 Massachusetts Avenue, N.W., Washington, D. C. 20005.

January 11–13: First International Conference on Prematurity. Pier 66, Ft. Lauderdale, Fla. Address: Mr. Wesley J. Duiker, Secretary, AMA Committee on Maternal and Child Care, 535 North Dearborn Street, Chicago, Ill. 60610.

January 14–18, 1968: Society for Cryo-Ophthalmology. Miami Beach, Fla. Address: Dr. John G. Bellows, Executive Secretary, 30 North Michigan Avenue, Chicago, Ill. 60602.

January 17–18: American Rheumatism Association. Baltimore. Address: Miss Margaret M. Walsh, 1212 Avenue of the Americas, New York, N. Y. 10036.

January 20–25: American Academy of Orthopaedic Surgeons. Palmer House, Chicago. Address: Mr. John K. Hart, 29 East Madison, Chicago, Ill. 60602.

February 6–10: American College of Radiology. Drake Hotel, Chicago. Address: Mr. William C. Stronah, Executive Director, 20 North Wacker Drive, Chicago, Ill. 60606.

**February 7–9: American Academy of Occupational Medicine. Marriott Twin Bridges Motel, Washington. Address: Dr. Bertram D. Dinman, Executive Secretary, Institute of Industrial Health, University of Michigan Medical Center, Ann Arbor, Mich. 48104.**

March 3–7: International Academy of Pathology. Drake Hotel, Chicago. Address: Dr. F. K. Mostofi, Secretary-Treasurer, IAP, c/o Armed Forces Institute of Pathology, Washington, D. C. 20305.

March 11–13: American College of Surgeons (Sectional Meeting for Doctors and Nurses). Williamsburg Inn, Williamsburg, Va. Address: Communications Department, 55 East Erie Street, Chicago, Ill. 60611.

March 13–15: International Symposium on Radiation Therapy. New York. Address: Dr. Ralph Phillips, Memorial Sloan-Kettering Cancer Center, 444 East 68th Street, New York, N. Y. 10021.

March 18–20: American Academy of Pediatrics. Regency Hyatt House, Atlanta, Ga. Address: Dr. Robert G. Frazier, Executive Director, 1801 Hinman Avenue, Evanston, Ill. 60204.

March 22–23: Second National Congress on the Socio-Economics of Health Care. Palmer House, Chicago. Address: Council on Medical Service, American Medical Association, 535 North Dearborn Street, Chicago, Ill. 60610.

March 29–31: American Society of Internal Medicine. Hotel Statler, Boston. Address: Mr. Edward E. Daleske, Assistant Executive Director, 3410 Geary Blvd., San Francisco, Calif. 94118.

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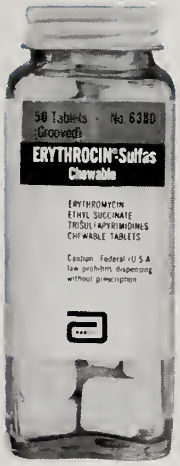
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In clinical trials[1,2], this orange-flavored tablet was given to 55 patients, aged four months to 18 years.

Diagnoses (multiple in some cases) represented a cross section of bacterial infections commonly seen in pediatric office practice.

Therapy was given from three to 12 days, with an average of six days.

Of the 55 patients, 30 were reported cured within 72 hours, while 22 showed partial recovery within the same time, and subsequent clinical cure.

**A clinical cure rate of 94.5%**

## ERYTHROCIN®-SULFAS Granules

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87 patients were treated[1,2]—all children, ages four months to 15 years.

The diagnoses were multiple in some cases and were chiefly bacterial infections of the respiratory tract.

Dosage was maintained from three to 10 days; average treatment was five days. All of the ill children accepted the orange-flavored suspension favorably.

53 were clinically cured within 72 hours, while 32 showed partial relief within the same time, and subsequent clinical cure.

701358

**A clinical cure rate of 97.7%**

ABBOTT

Brief
Summary
on next
page

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1. Case Reports on File, Dept. Clin. Development, Abbott Laboratories.
2. Polley, R.F.L., Use of Erythromycin-Sulfas in Office Practice, Western Med., 7:177, July, 1966.

## ERYTHROCIN®-SULFAS
Brief Summary

**Contraindications:** Known sensitivity to erythromycin or sulfonamides. Because of the possibility of kernicterus with sulfonamides, do not use in pregnancy at term, premature or newborn infants.

**Warnings:** As with other forms of sulfonamide therapy, carefully evaluate patients with liver or kidney damage, urinary obstruction, or blood dyscrasia. Deaths have been reported from hypersensitivity reactions and blood dyscrasias following use of sulfonamides. Perform blood counts and liver and kidney function tests if used repeatedly at close intervals or for long periods.

**Precautions, Side Effects:** Occasionally mild abdominal discomfort, nausea or vomiting may occur with erythromycin, generally controlled by reduction of dosage. Mild allergic reactions (such as urticaria and other skin rashes) may occur. Serious allergic reactions have been extremely infrequent. Use sulfonamides with caution in patients with a history of allergy. Assure adequate fluid intake to prevent crystalluria and institute alkali therapy if indicated. If overgrowth of nonsusceptible organisms occurs, withdraw the drug and institute appropriate treatment. If a patient should show signs of hypersensitivity, appropriate countermeasures (e.g. epinephrine, steriods, etc.) should be administered and the drug withdrawn.

**Adverse Reactions:** Sulfonamide therapy may be associated with headache, nausea, vomiting, urticaria, diarrhea, hepatitis, pancreatitis, blood dyscrasias, neuropathy, drug fever, skin rash, injection of the conjunctiva and sclera, petechiae, purpura, hematuria and crystalluria.

Side effects due to erythromycin are infrequent, but occasional abdominal discomfort, nausea, or vomiting, urticaria and other skin rashes may occur.

**Supplied:** The Granules for Oral Suspension come in bottles of 60 ml. and 150 ml. The Chewable tablets are in bottles of 50. Each 5-ml. teaspoonful of reconstituted Granules or each Chewable tablet provides erythromycin ethyl succinate equivalent to 125 mg. of erythromycin activity and 167 mg. of each of sulfadiazine, sulfamerazine and sulfamethazine.

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His teen-age granddaughter won't invite friends home because of his outbursts.

for moderate to severe anxiety

**Mellaril®**

**(thioridazine)**

**25 mg. t.i.d.**

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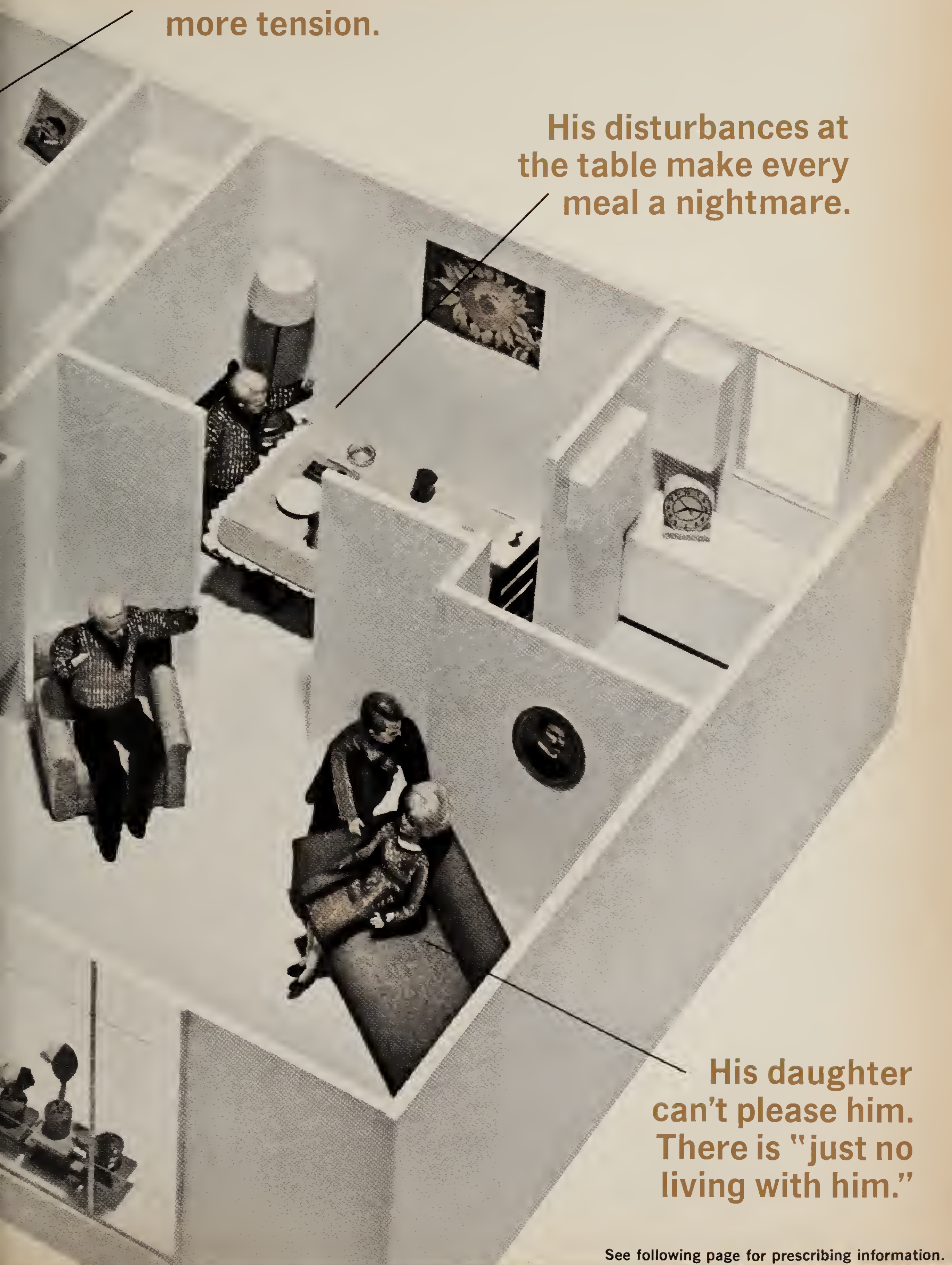

His slovenly room and habits create more tension.

His disturbances at the table make every meal a nightmare.

His daughter can't please him. There is "just no living with him."

See following page for prescribing information.

## When the agitated geriatric disrupts the home...

Anxiety that *seriously interferes* with the individual's performance at work, at home, or in the community may be regarded as *moderate* to severe in degree.

Mellaril often recommends itself to the treatment of moderate to severe anxiety because it

- helps control the most frequent symptoms: marked tension, agitation, apprehension, restlessness, hypermotility
- often alleviates anxiety-induced somatic complaints
- frequently helps strengthen emotional resources
- helps the patient maintain realistic contact with environment, closer harmony with family

Thus, when you consider the anxiety moderate to severe... consider Mellaril.

**Contraindications:** Severely depressed or comatose states from any cause, and in association with or following MAO inhibitors; severe hypertensive or hypotensive heart disease.

**Precautions:** Hypersensitivity reactions (e.g., leukopenia, agranulocytosis) and convulsive seizures are infrequent. Pigmentary retinopathy has been observed where doses in excess of those recommended were used for long periods of time. May potentiate central nervous system depressants, atropine, and phosphorus insecticides. Where complete mental alertness is required, administer the drug cautiously and increase dosage gradually. In addition, orthostatic hypotension (especially in female patients) has been observed. Epinephrine should be avoided in treatment of drug-induced hypotension.

**Side Effects:** Pseudoparkinsonism and other extrapyramidal disorders are infrequent; drowsiness, especially in high doses early in treatment, may occur; nocturnal confusion, dryness of the mouth, nasal stuffiness, headache, peripheral edema, lactation, galactorrhea, and inhibition of ejaculation are noted on occasion; photosensitivity and other allergic skin reactions may occur but are extremely rare.

*Before prescribing,* see package insert for *full product information.*

**for moderate to severe anxiety**

**Mellaril®**
**(thioridazine)**
**25 mg. t.i.d.**

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**The fast-disintegrating uncoated tablet gives relief in 15 minutes**

*Each tablet contains:*

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Precautions: Usual for aminophylline-ephedrine-phenobarbital. Iodides may cause nausea, long use may cause goiter. Discontinue if symptoms of iodism develop.

Iodide contraindications: tuberculosis, pregnancy.

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| Dextromethorphan hydrobromide | 30 mg. |
| Terpin hydrate | 180 mg. |
| Acetaminophen | 325 mg. |

Dosage: Adults—1 tablet, swallowed whole to preserve timed-release feature, in morning, midafternoon and at bedtime. Side effects: Occasional drowsiness, blurred vision, cardiac palpitations, flushing, dizziness, nervousness or gastrointestinal upsets. Precautions: The patient should be advised not to drive a car or operate dangerous machinery if drowsiness occurs. Use with caution in patients with hypertension, heart disease, diabetes or thyrotoxicosis.

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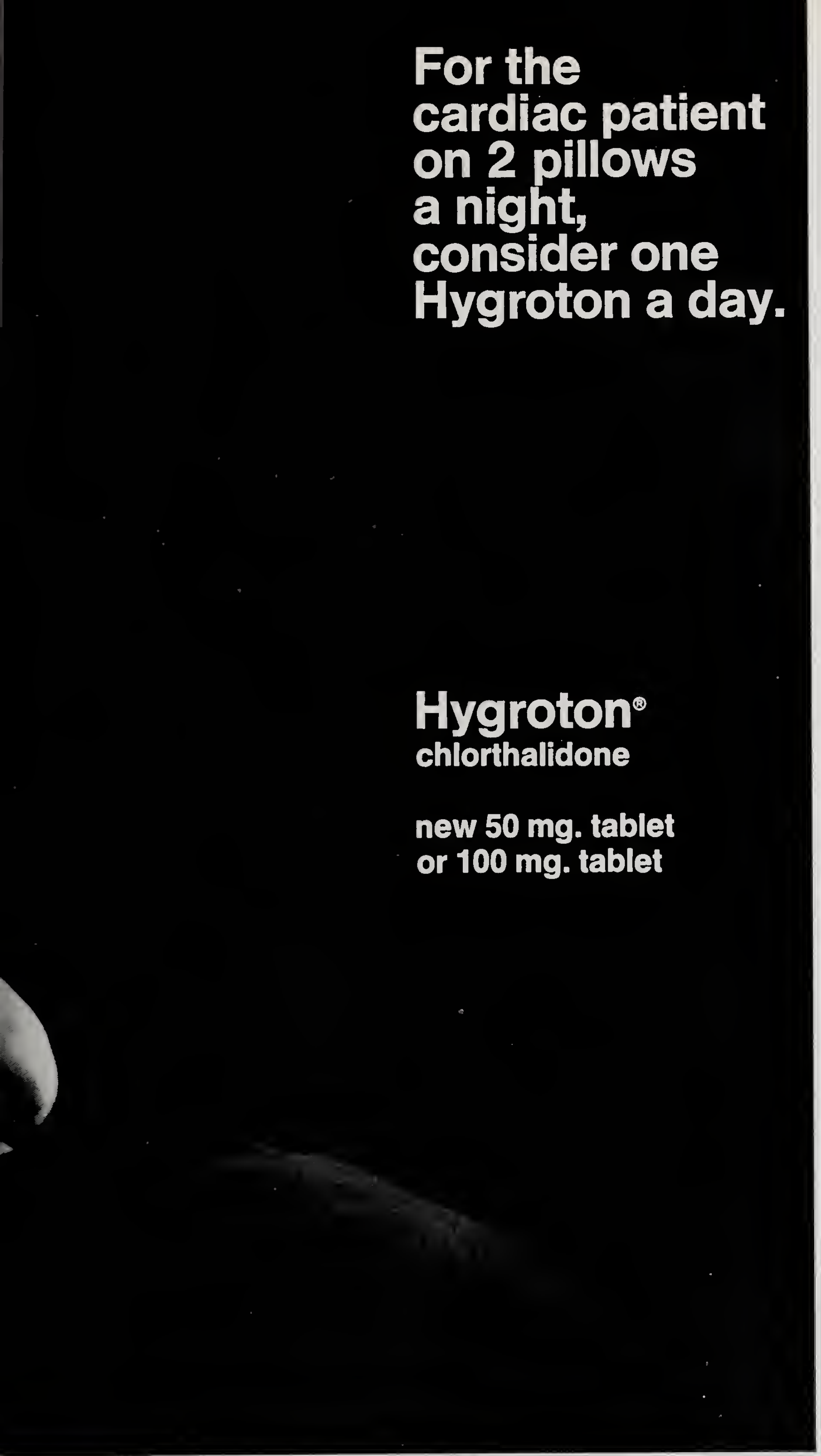
**Warning:** With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery for these lesions has frequently been required and deaths have occurred. Discontinue enteric-coated potassium supplements immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur.
Use with caution in pregnant patients, since the drug may cross the placental barrier and adverse reactions which may occur in the adult (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential problems in the newborn.
**Precautions:** Antihypertensive therapy with Hygroton should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents or other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. Barbiturates, narcotics or alcohol may potentiate hypotension. Because of the possibility of progression of renal damage, periodic determination of the BUN is indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated.
Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Hygroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria.
Take special care in cirrhosis or



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She couldn't sleep a wink without an extra pillow.
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**new 50 mg. tablet**
**or 100 mg. tablet**

severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended.
**Adverse Reactions:** Nausea, gastric irritation, vomiting, anorexia, constipation and cramping, dizziness, weakness, restlessness, hyperglycemia, hyperuricemia, headache, muscle cramps, orthostatic hypotension, aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, impotence, dysuria, transient myopia, skin rashes, urticaria, purpura, necrotizing angiitis, acute gout, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Other reactions reported with this class of compounds include: jaundice, xanthopsia, paresthesia, and photosensitization.
**Average Dosage:** 50 or 100 mg. with breakfast daily or 100 mg. every other day.
**Availability:** White, single-scored tablets of 100 mg. and aqua tablets of 50 mg., in bottles of 100 and 1000.
(B)R46-230-D
**For full details, please see the complete prescribing information.**

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MEDICAL ANNALS

*of the District of Columbia*

*December 1967* VOLUME XXXVI • NUMBER 12

# Recent Developments Concerning the Pathology and Pathogenesis of Ocular Malformations in Rubella*†

LORENZ E. ZIMMERMAN, M.D.‡

To pay tribute to 3 such great men in the medical history of our country as Theobald Smith, Walter Reed, and Frederick Russell by delivering a lecture in their memory is an honor that anyone would be eager to accept. For me it was particularly gratifying to receive the invitation. Being a Washingtonian and twice a graduate of The George Washington University, I am especially pleased to be able to pay homage to these men who contributed so much toward placing Washington, D. C. and The George Washington University on the map, medically speaking. Adding to this personal pleasure is the fact that I was once a member of the Smith-Reed-Russell Honor Society (never suspecting that one day I might be addressing the Society!).

Having been an Army Medical Officer or otherwise in Government service ever since graduation from this Medical School, I can be particularly proud of the fact that Smith, Reed, and Russell all came to Washington in the service of our country and established their reputations as a result of that service. I am also proud of the fact that already in those early days at the turn of the century the Federal Government and the University had joined forces in advancing medical education, a tradition that fortunately has continued to the present.

The Army Medical Museum in particular was closely related to this Medical School. Of interest along these lines is the fact that during the period 1863–1866 the Museum occupied this building, then called the Corcoran School.[1] In 1867 the Museum moved into Ford's Theater, where Lincoln had been assassinated, and Mr. Corcoran gave this building to the Medical School, which now celebrates its centennial of occupancy.[2]

For the benefit of those of you who as yet may not have learned anything of Smith, Reed, and Russell I should like to say a few words about their relationship to this School of Medicine. Theobald Smith, who came to Washington in 1884 at the age of 25 to direct the laboratory of the Bureau of Animal Industry, 2 years later occupied the first Chair of Bacteriology at an American medical school here at G.W.[2] During the 10-year period of his professorship Smith did his pioneer work on tick fever and bovine tuberculosis.

Walter Reed, probably the most famous of these 3 great men, taught pathology and bacteriology at G.W. while he was Curator of the Army Medical Museum, the institution that subsequently matured into the Armed Forces Institute of Pathology. Walter Reed taught here during the period (1901–1902) immediately following his successful direction of the Yellow Fever Commission which established the *Aedes aegypti* as the transmitter of yellow fever.[1]

When Walter Reed died prematurely of the effects of appendicitis in November 1902 he was succeeded as Curator of the Army Medical Museum by his very close associate, Lt. James

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* Annual Lecture, presented before the Smith-Reed-Russell Medical Society, an honor society of George Washington University School of Medicine, April 20, 1967.

† The work reported in this paper was supported in part by Public Health Service Training Grant 5 T1 NB 5379-05 from the National Institute of Neurological Diseases and Blindness, National Institutes of Health, Public Health Service, United States Department of Health, Education, and Welfare.

‡ Chief, Ophthalmic Pathology Branch, Armed Forces Institute of Pathology, Washington, D. C. 20305.

Carroll. Carroll had served on Reed's Yellow Fever Board, and he, too, upon their return from Panama, served on the faculty of this Medical School, teaching pathology and bacteriology.[1, 2] It has always seemed strange to me that the founders of the Smith-Reed-Russell Society did not see fit to honor also the name of Carroll.

Carroll died in 1907 and was succeeded by Captain Frederick Fuller Russell as Curator of the Museum and Professor of Bacteriology and Clinical Microscopy at the Army Medical School. His outstanding achievement was the development of a typhoid vaccine for the Army. This work was also done at the Army Medical Museum, where human volunteers on the Museum staff permitted themselves to be used to test the vaccines. Two years later (in 1911) vaccination against typhoid was made compulsory for the entire Army, and by the end of the year 85 per cent of all personnel had been immunized.[1] During this same period Russell served as Professor of Pathology and Bacteriology at G.W.[2]

The subject that I have selected for this Smith-Reed-Russell Lecture is appropriate for the occasion, as it illustrates again the interdependency of research microbiologists, pathologists, and clinical investigators engaged in research into the solution of intriguing medical problems related to infectious diseases.

In 1941 Norman Gregg,[3] an Australian ophthalmologist, reported on observations that he and his colleagues had made on infants born during the year that followed the large outbreak of rubella that spread through Australia during 1940. Congenital cataract was the most striking and most frequent lesion that directed Gregg's attention to the possible role of a maternal history of rubella. The cataracts were distinctive, dense nuclear opacities and were unlike other well-recognized varieties of congenital cataract. They were usually bilateral, but in one-fifth of the cases they occurred unilaterally. In many of these unilateral cases the cataractous eye was slightly smaller than the noncataractous eye. Gregg noted that the irides often appeared atrophic and that full mydriasis was difficult or impossible to obtain. He mentioned one case in which ophthalmoscopic examination of the noncataractous eye of a child with unilateral cataract revealed a peculiar pigmentation of the ocular fundus. In addition to these and other impressive ophthalmologic findings, such as congenital glaucoma and corneal opacification, Gregg observed that most of the babies were small, ill-nourished, and difficult to feed. Fifteen babies died. Many were found to have evidence of congenital heart disease, and subsequent studies revealed a high incidence of deafness and mental retardation.

It did not take long for Gregg's paper to receive worldwide recognition, and his clinical observations were soon confirmed, not only by his Australian colleagues[4] but also by physicians the world over.[5, 6, 7] Thus was born the concept that this typically benign exanthematous disease, German measles, when occurring early in pregnancy might lead in some mysterious way to the development of a wide variety of malformations in the patient's baby.

Until recently, however, little was learned about the pathologic anatomy of congenital rubella, and its pathogenesis was merely a matter for speculation. During the 2 decades that followed Gregg's report basic research was limited by the facts that the causative agent of rubella was unknown and that there was not a suitable laboratory model for study of the disease in experimental animals. Congenital rubella remained a mysterious entity until very recently, when in quick succession 2 important events occurred. The first of these was the recovery of the rubella virus. In 1962 Parkman and co-workers[8] at the Walter Reed Army Institute of Research and Weller and Neva[9] at Harvard's School of Public Health independently and simultaneously recovered an agent that was shown to cause rubella. Sever and his associates[10] at NIH quickly provided confirmation that this new infectious agent is the cause of rubella and that it is a virus.

The second major event that immediately stimulated a fantastic amount of clinical, laboratory, and epidemiologic investigation was the occurrence of numerous large outbreaks of rubella during the winter of 1963–1964.

Before the causative virus of rubella was recovered there was no way that one could be absolutely certain whether a patient did or did not have rubella. In the case of the physician trying to make a retrospective diagnosis of maternal rubella because of a baby born with congenital malformations the difficulties were even greater. Furthermore, soon after Gregg's initial report it became apparent that mothers who had never had clinical evidence of rubella during their pregnancy might still give birth to babies with malformations typical of those associated with maternal rubella. In addition to these difficulties there was the knowledge that malformations (including congenital cataracts) due to causes other than rubella may be difficult to distinguish from those caused by maternal rubella. Thus the ophthalmic pathologist had no reliable criteria by which he could be reasonably certain whether any given ocular malformation he might be called upon to study was or was not the result of maternal rubella.

Today, just 5 years after the rubella virus was first described, data from hundreds of cases confirmed by recovery of the virus have been accumulated, and a wealth of information relative to the pathogenesis of congenital rubella now clearly reveals it to be a disease that is very different from acquired rubella. The latter is typically a mild exanthematous disease of short duration. The virus is present before the rash appears but persists only a short while in the pharyngeal secretions (rarely as long as 2 weeks) after the onset of the rash. The virus disappears from the blood during the first 48 hours as specific neutralizing antibody makes its appearance.[11, 12] The latter is believed to persist permanently and to protect against reinfection.

Congenital rubella, on the other hand, being acquired so early in gestation before the fetus has developed the immunologic defense mechanisms that seem so effective in protecting the tissues against the virus after birth, is characterized by widespread cellular parasitism of the host's tissues.[13-19] The virus is believed to become incorporated into the infected cells' DNA, where it may compete with the latter for various metabolites in its replication.[20] Rawls and co-workers[18, 19, 21] have shown that cells grown in tissue culture obtained from various organs at autopsy are infected, yet these infected cells appear to be normal cytologically. No cytopathogenic effect of the virus is observed. The virus does retard cell division, however, and the infected tissues grow more slowly. This is believed to account for the fact that rubella babies are typically of subnormal weight and that they fail to thrive after birth.[19, 22] Once having invaded various tissues so early in embryologic development, the virus in its protected position within the cells persists in these tissues not only throughout gestation but for as long as a year and a half or more after birth. Not only does the virus persist, but it replicates as the cells divide. Rawls and co-workers[19] have shown that from a single infected cell it is possible to develop clones in which every cell is infected. Presumably this occurs in many human tissues, since the virus has been recovered from nasopharyngeal secretion, urine, feces, cerebrospinal fluid, aqueous humor, and many tissues, including the lens, obtained surgically or postmortem. The overall effect of widespread cellular parasitism by this virus on the baby is demonstrated by the positive correlation of prolonged excretion of virus and the failure of infants to thrive after birth; the smaller the baby and the less its weight gain after birth, the greater the excretion of virus.[19]

Early estimates of the frequency of various malformations attributable to maternal rubella during the first 2 months of gestation were inordinately high (80 to 100 per cent) because they were based on retrospective studies.[4, 23, 24] Recent prospective studies would indicate the risk to be much lower—in the neighborhood of 10 to 20 per cent. [24, 25, 26] All reports, however, have been in general agreement that the greatest danger to the embryo is during the first 4 to 8 weeks and that cataracts are among the most frequently observed complications.

Because of the fact that there is an appreciable mortality among rubella babies, a number of postmortem studies have been made on babies who have died since the epidemic of 1963–64.[27, 28] In many of these cases the rubella virus was recovered antemortem from the throat, urine, feces, or other tissues, or it was recovered from 1 or more tissues or body fluids at the time of autopsy. Fortunately, the eyes were also removed for histopathologic study in many of these proved cases of congenital rubella. Dr. Milton Boniuk of Baylor University and I[28] collected 26 eyes from 17 cases in which the diagnosis of congenital rubella was confirmed by virus isolation (15 cases) or serologic studies (2 cases).

Our most consistent finding was one that few others have observed or recorded. In almost every one of our cases there was either an active iridocyclitis or evidence of its sequelae (figure 1). Areas of degeneration or discrete punched-out areas of necrosis of the pigment epithelium of the ciliary body were observed in almost every eye, even in those without cataract or glaucoma. In the stroma adjacent to these lesions one could see evidence of dispersion of pigment with phagocytosis by macrophages. Pigmented macrophages were also observed in the posterior chamber attached to the surface of the ciliary epithelium in the vicinity of these lesions. In addition to the stromal infiltration of the iris and ciliary body by lymphocytes, plasma cells and histiocytes, these cells could also be observed in the posterior chamber.

Other very characteristic changes observed in the anterior uvea included the vacuolization of the pigment epithelium of the iris, severe stromal atrophy, and absence or severe hypoplasia of the dilator muscle. This, of course, provides an explanation for the difficulty Gregg noted in obtaining good dilation of the pupil. Incomplete

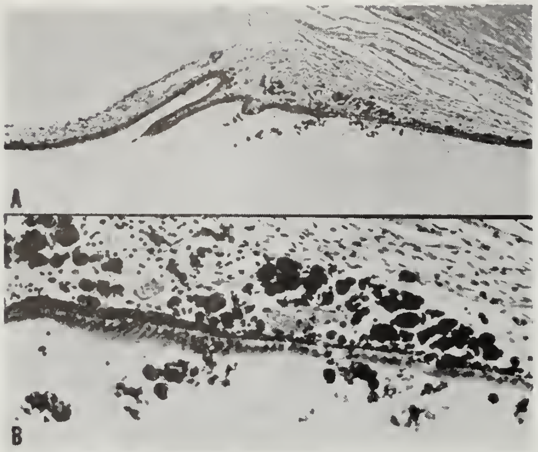

**FIG. 1. A.** Mild to moderate nongranulomatous iridocyclitis, one of the most constant features observed in the eyes of babies who died as a result of sequelae of congenital rubella. **B.** Focal areas of necrosis in pigment epithelium of ciliary body with dispersion of pigment and melanophagic activity are other highly characteristic features (AFIP Neg. 65-3968).

differentiation of the anterior chamber angle was present in many of these eyes (figure 2). This readily explains the congenital glaucoma that may mimic familial congenital glaucoma.[29]

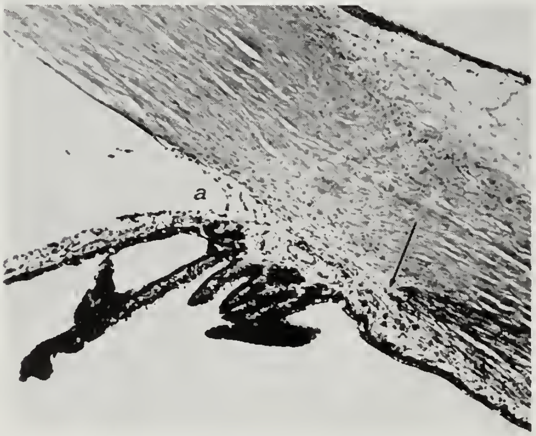

**FIG. 2.** Marked retardation in cleavage of anterior chamber angle, shown at "a"; normally the chamber angle is located near the tip of the arrow, just anterior to the ciliary muscles (AFIP Neg. 67-2307).

We had 15 cataractous lenses for histopathologic study, and in 13 of these the lens appeared tumid or spherophakic (figure 3*). The 2 with a more normal contour revealed only minimal cortical degeneration (figure 4), while the others exhibited variable degrees of necrosis and lique-

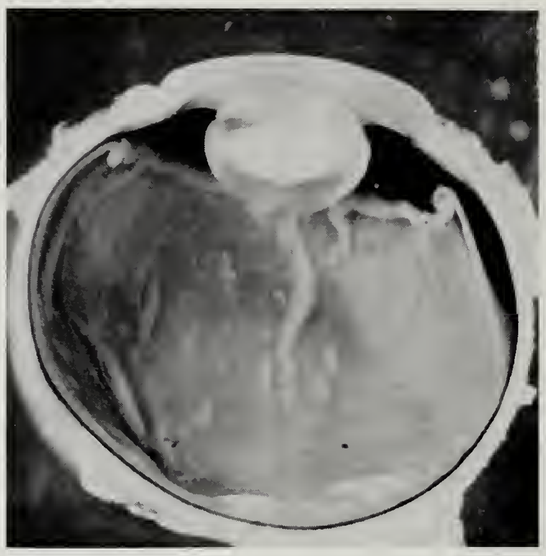

**FIG. 3.** Very dense nuclear cataract, which appears pearly white. The less dense but also opaque cortical area is swollen, giving the lens a markedly increased anteroposterior diameter and an almost spherical contour (AFIP Neg. 65-3166-6).

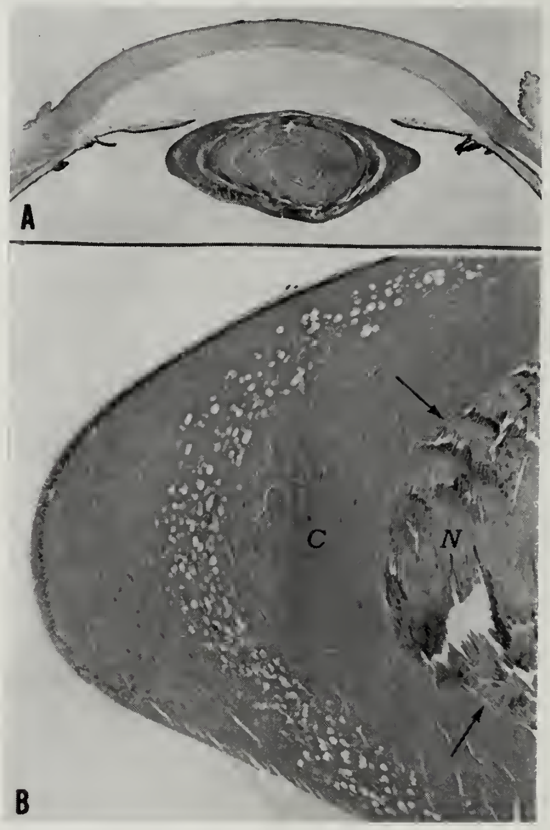

**FIG. 4. A.** Dense nuclear cataract, with cortex relatively uninvolved and shape of lens only slightly abnormal (AFIP Neg. 65-3960). **B.** Arrows indicate abrupt change from essentially normal cortex (C) to markedly sclerotic nucleus (N) (AFIP Neg. 65-1034).

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* Figure 3 was supplied by Dr. Milton Boniuk, Department of Ophthalmology, Baylor University, Houston, Texas.

faction of cortical cells (figure 5). Often, however, an equatorial rim of relatively normal cortical fibers was present even in those cases with advanced cortical degeneration and liquefaction necrosis. A remarkable feature—one distinguishing these congenital cataracts from those observed in many other conditions (e.g., 13–15 trisomy, Lowe's syndrome, Miller's syndrome, Down's syndrome)—was the relatively normal appearance of the lens epithelium and capsule. Conspicuous by their absence were the posterior migration of lens epithelium and the hyperplasia and metaplasia of the anterior polar cells observed so frequently in many forms of congenital and acquired cataract.[27] Another typical feature not previously appreciated for its diagnostic significance was the persistence of cellular outlines and nuclei in the central mass of densely opaque lens tissue, which normally appears homogeneous and is free of cell nuclei (figure 6). The persistent nuclei are typically karyorrhectic, resembling superficially polymorphonuclear leukocytes, but they may also appear as pyknotic or karyolitic structures. The combination of features we have described in these lenses is believed to be virtually pathognomonic of rubella cataracts.

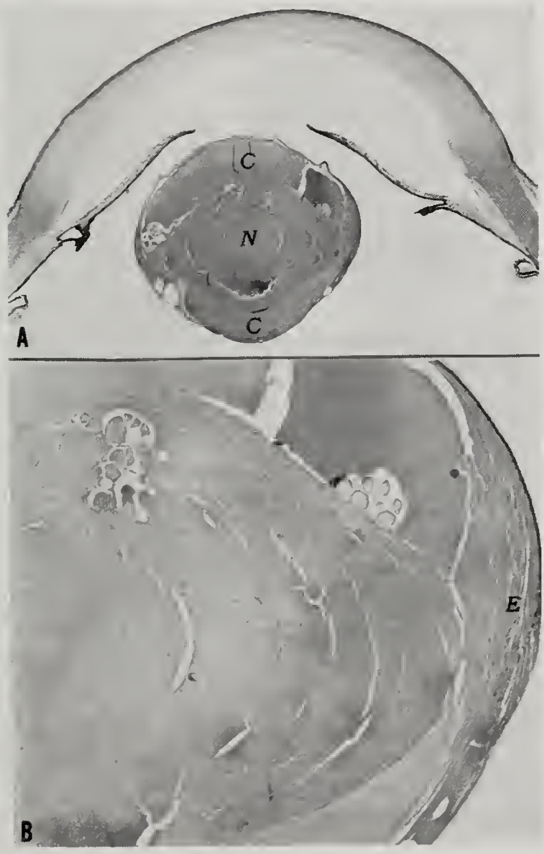

**FIG. 5. A. Intumescent lens exhibiting advanced liquefaction necrosis of cortex (C) as well as sclerosis of nucleus (N) (AFIP Neg. 65-3966). B. At extreme periphery in equatorial region (E) there are some relatively normal, recently formed cortical fibers (AFIP Neg. 65-3972).**

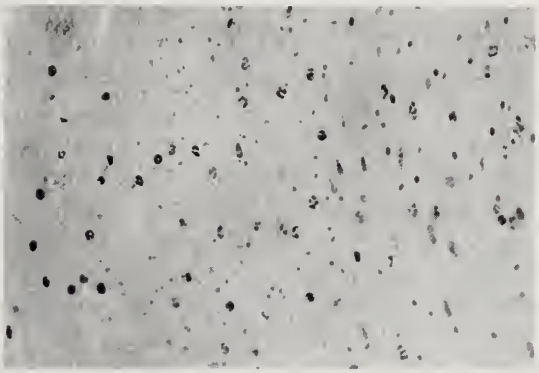

**FIG. 6. Retention of cell nuclei, which appear karyorrhectic and resemble polymorphonuclear leukocytes, in densely sclerotic center of rubella cataract. Normally cell nuclei are observed only in the equatorial cortex (area E in figure 5-B), while the deeper cortical tissue and the lens nucleus are devoid of visible cell outlines and nuclei (AFIP Neg. 65-5251).**

Our studies have also provided an explanation for the peculiar appearance of the ocular fundus. Posteriorly one sees degeneration of the retinal pigment epithelium with variable loss of pigment granules.

Significant by their absence were marked microphthalmia and the various severe malformations that are often associated with profound microphthalmia such as colobomas, retinal dysplasia, orbital cysts, and persistent hyperplastic primary vitreous.

From these observations I have proposed minimal criteria for the histopathologic diagnosis of congenital rubella infections of the eye.[30] Two or more of the following features should be observed:

1. Chronic nongranulomatous iridocyclitis with focal necrosis of pigment epithelium of the ciliary body.
2. Nuclear or total cataract with retention of karyorrhectic nuclei in lenticular cells centrally and absence of noteworthy changes in lens capsule or epithelium (except following surgical procedures).
3. Absence of severe microphthalmia, colobomas, retinal dysplasia, and other more profound disturbances of ocular development.

Application of these criteria for histopathologic diagnosis has enabled us to make the diagnosis of ocular malformations caused by rubella in a reveiw of old cases on file in the Registry of Ophthalmic Pathology. It has also permitted us to exclude the possibility of rubella in certain cases in which, for one reason or another, it had been considered a possible cause of ocular malformations.[30]

### Implications for Future Research

It has been the experience of pathologists who have studied the general effects of congenital rubella on tissues other than the eyes that the virus produces little evidence of necrosis and provokes no inflammatory response.[31] We, on the other hand, have found an infiltrate of lymphocytes and plasma cells in the anterior uvea to be one of the most frequent findings, along with foci of necrosis in the pigment epithelium. It would seem that the rubella virus may exhibit a particular tropism for the pigment epithelium. Whether the uveitis represents an immunologic response to the virus itself or a more nonspecific reaction to necrosis of the pigment epithelium remains to be determined. It seems fairly certain that the uveitis is not lens-induced, because we have observed the iridocyclitis in eyes with clear lenses. Use of the fluorescent-antibody technique might settle the question, for if my suspicion is correct, the plasma cells observed in the iris and ciliary body should contain antirubella antibody. I do not know whether anyone has attempted such studies. Ideally, the eyes should be relatively fresh and frozen rather than fixed in formalin for such immunofluorescent investigations. By these techniques it has already been shown that the presence of the virus can be demonstrated in tissues that appear histologically to be quite normal,[32] but again I am not aware of a similar study of the human ocular tissues. I would suspect that perhaps the retinal pigment epithelium might reveal a particularly dense accumulation of the virus.

The retention of nuclei in the dense central part of the lens, where normally and in most other types of congenital cataract the tissue is completely acellular, is an observation that is not only of diagnostic value but also of potential theoretical implications. If the rubella virus does indeed become incorporated in the DNA of the lenticular cells, it may alter the physicochemical properties of the nucleoproteins in such a way that there is an interference with the normal karyolysis that leads to a disappearance of nuclei in all but the outer cortical fibers of the lens. This is a subject that should be of great interest to those investigators who are particularly interested in the chemical and enzymatic aspects of the lens.

Parkman and co-workers[33, 34] have shown that the rhesus monkey is a sensitive, susceptible host for studying experimental infection with rubella virus. At the time of their last report they had been able to produce transplacental infections in their pregnant monkeys but had not yet succeeded in producing anatomic abnormalities.

Dr. Cotlier and his associates[35] at Washington University have succeeded in producing a convenient laboratory model that should permit a detailed investigation of many intriguing problems. They have reproduced the congenital rubella syndrome in the rat, with (1) a high incidence of neonatal deaths, (2) low birth weight and retarded growth, (3) cyanosis and possible cardiac anomalies, (4) purpura, and (5) cataracts. Their as yet unpublished light and electron microscopic studies are said to have shown "selective damage to the nuclei of epithelial cells and developing lens fibers. The cytoplasm and cytoplasmic organelles of the lens cells remained untouched." A suggestion of virus particles was observed in some nuclei by electron microscopy, and immunofluorescent techniques have provided confirmatory evidence of the presence of virus within the damaged lenses.

Studies at Baylor[36] have shown that the rubella virus not only produces about a 2-fold increase in the doubling time of cells in tissue culture during the early phase of accelerated growth, but they have also demonstrated the progressive effect that the intracellular virus has on these cell lines. Normal cells in culture can undergo about 50 cell divisions before the line dies out. Cells infected with rubella last only about half as long. It would be of interest to see how much variation in this time there might be with different cell lines. Is the effect the same on lens epithelium and pigment epithelium as on other cell lines? Why does the virus produce a relatively greater damage to lens epithelium than to retinal pigment epithelium? Does the virus do less damage to nondividing cells than to those that proliferate more rapidly? Is the relatively greater tissue damage observed in the lens attributable to its greater isolation from circulating antibody?

The question has also arisen as to whether chromosomal aberrations might not play a role in the pathogenesis of malformations in congenital rubella. Chang and co-workers,[37] who made an extensive study of this possibility, found a marked elevation in frequency of chromosome breakage in cell strains obtained from 3 of 17 fetuses and a slight but significant elevation in the average frequency in 4 cell strains that had been experimentally infected in vitro with rubella virus. Although these effects upon the chromosomes were demonstrated, the authors were nevertheless of the opinion that the fetal abnormalities were more likely the consequence of the effects of the virus upon cell growth. Their in vitro studies utilized cultured fibroblasts, and, as the authors pointed out, it is possible that the chromosomal effects on other cell types might be significantly different.

## Summary

For 20 years following the first publication by Gregg,[3] Swan,[4] and their Australian colleagues no significant advances were made toward establishing the pathogenesis of malformations resulting from congenital rubella infection. Recovery of the virus and the development of microbiologic methods for detection of rubella infection in asymptomatic subjects and in newborn babies, followed almost immediately by this country's first massive epidemics of the disease in many years, permitted the acquistion of an amazing amount of information and tremendous advances in our knowledge of the pathologic anatomy and pathogenesis of ocular changes caused by maternal rubella.

Now it is firmly established that the ocular malformations observed in rubella babies are the result of actual infection of the affected tissues of the eye and that this infection may persist for months after birth. The infection is characteristically accompanied by a low-grade uveitis that had not previously been recognized as a typical clinical feature of congenital rubella.

Microscopic examination of the eye has established a number of histopathologic characteristics that should prove useful in distinguishing congenital cataracts and glaucoma caused by rubella from similar malformations caused by other factors.

Application of general principles that have been elucidated concerning the effects of the rubella virus on cell growth and function to the teratogenic effect of maternal rubella has largely accounted for many of the mysterious aspects of Gregg's syndrome, but there still remain certain problems for future research to answer. The development of the congenital rubella syndrome in laboratory animals should provide a welcome substitute for the serendipitous accumulation of knowledge that has characterized advances of the past few years.

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# Photosensor Monitoring of Supraorbital Blood Flow*

## A New Approach to the Detection and Diagnosis of Carotid Occlusive Disease

WILLIAM L. HOWELL, M.D.†

INTEREST IN THE supraorbital arterial circulation as a possible site for the detection of carotid occlusive disease was aroused by the report of Heyman[1] that in certain subjects the skin temperature in the supraorbital area on the ipsilateral side of carotid artery stenosis was reduced as demonstrated by infrared thermography. Our own studies suggest that this was a chance finding and that blood flow to these areas is promptly normalized by the development of abundant collaterals. With a new dynamic method of photosensor monitoring I have been able to identify such collaterals readily by manual compression. Moreover, a response pattern which appears to be peculiar to unilateral carotid artery stenosis follows manual compression of the carotid arteries in the neck.

The application of photoelectric methods to the study of the peripheral circulation in the skin is not new. Hertzman[2] used the method in the study of the blood volume pulse (BVP) and the blood volume (BV) in the periphery by measuring the light intensity after transluminating a limb or after reflecting the light from different areas of the skin. Similar results on human skin were obtained by Pauli and Ivančević.[3] Technical aspects of the method have been recently explored in depth by Weinman and Manoach.[4] Although the photoelectric method was suggested as possibly being useful in the estimation of supraorbital blood flow during the Fifth International Conference on Cerebral Vascular Disease, 1965,[5] the only reference to its use in the study of the cerebral circulation is that of Groveman et al[6] which involved pulse monitoring via the nasal septum.

### Equipment and Procedure

Paired sensors, designed to provide a disc-shaped surface for skin contact, consist of a centrally placed cadmium sulfide photoresistor sensitive to green light mounted in a cylindrically shaped plexiglass light pipe and surrounded by a cover of dark rubber.‡ Illumination is provided by an incandescent light source intercepted by a Wratten No. 58 green filter. Circuitry includes a stabilized power source and a means for amplification. The light enters tissues peripherally, carried by the plexiglass light pipe. Light reflected through the tissues reaches the photosensor and changes its resistance, which is measured through a Wheatstone bridge arrangement and may be graphically presented on an oscilloscope or be recorded. With decreased blood flow to the skin and subcutaneous tissues absorption of the green light will decrease and more light will reach the photosensor.

For examination, subjects are placed in a supine position with their head elevated 15° to 20°. In this position the pulse wave amplitude is increased because of a more rapid venous return. The paired sensors are secured to the skin in each of the 2 supraorbital areas (we have empirically centered these 2 cm. from the midline and 2 cm. above the supraorbital margin) with interposed translucent transfer adhesive (Scotch Pressure Sensitive Tape No. 465), thereby avoiding local tissue distortion. Collateral contribution to the arterial blood supply to the area is assessed by compressing in turn the angular arteries at the base of the nose and the superficial temporal arteries just anterior to the tragi of the ears. Contribution by the occipital artery may be detected by placing an elastic band about the head or by suspending the head over a band hammock. Following identification of collaterals the carotids in turn are compressed in the neck.

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* Supported by the James F. Mitchell Foundation, Washington, D. C.

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‡ Instrumentation by Prototypes, Inc., Kensington, Maryland.

### Results

Records obtained from normal young persons have shown no reduction in wave amplitude during compression of adjacent arteries. Responses to carotid compression have shown slowing of the pulse rate in some, but wave amplitudes have remained comparable. In normal older persons varying degrees of depression of wave amplitude have been observed after compression of the superficial temporal, angular, or occipital arteries. In all subjects having internal carotid artery stenosis, as demonstrated by arteriography, the presence of collaterals was shown by the reduction of pulse-wave amplitude as observed after elimination of collateral flow by manual compression (figure 1).

All subjects examined to date having unilateral carotid artery stenosis have not only exhibited the presence of collaterals to the supraorbital area but also have shown identical patterns of response to common carotid artery compression. When the maneuver is carried out on the ipsilateral side of the lesion the pulse wave from the opposite supraorbital field shows either no reduction in amplitude or may be increased, particularly if the pulse rate is slowed by the carotid sinus effect (figure 2). Manual compression of the common carotid artery on the contralateral side has shown marked changes in pulse waves recorded from both supraorbital

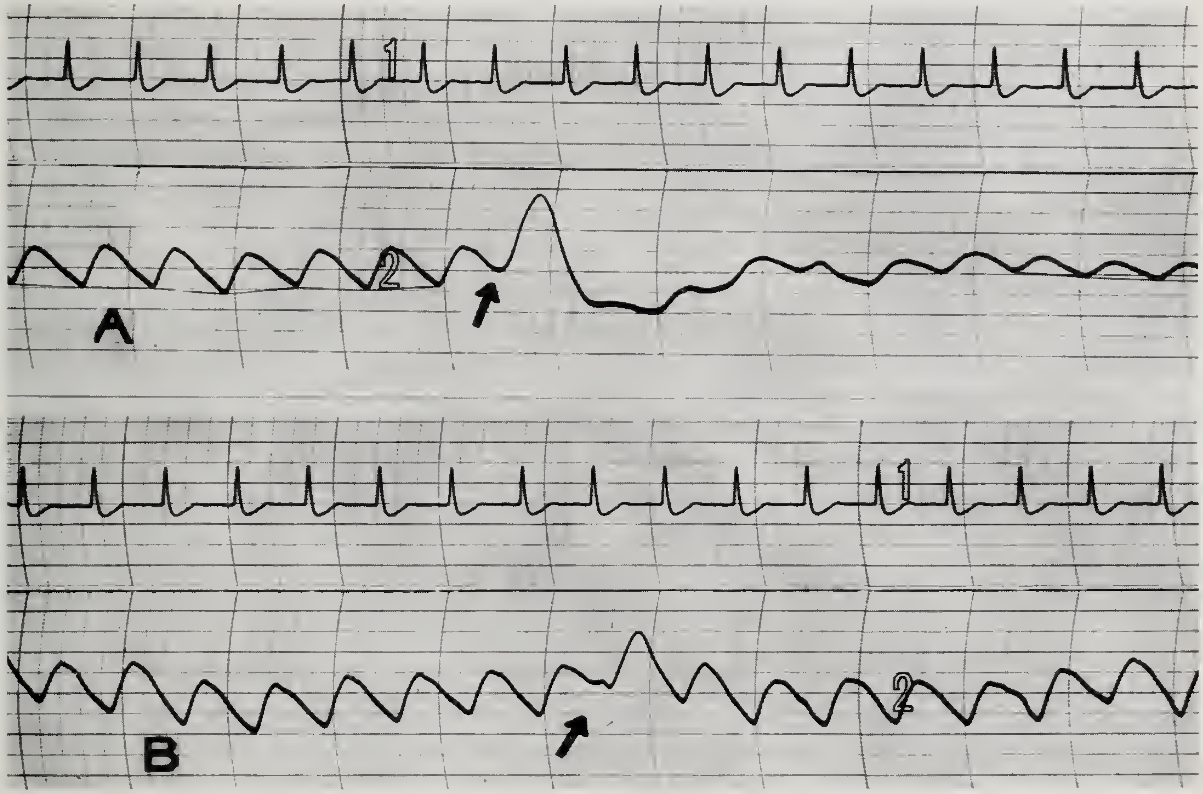

**FIG. 1. Tracings showing pulsatile flow to left (A) and right (B) supraorbital areas in a 75-year-old person with stenosis of left internal carotid artery. Compression of right superficial temporal artery produced no change whereas compression of the left superficial temporal artery caused the pulse wave from that side to be flattened and delayed, suggesting that blood flow was then via a stenosed internal carotid artery.**

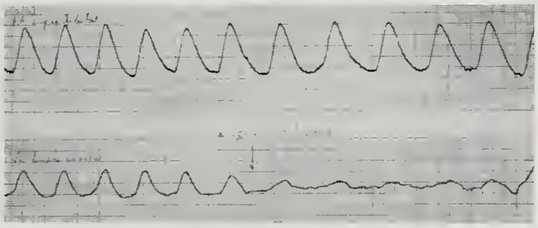

**FIG. 2. Manual compression of the left common carotid artery on the ipsilateral side of stenosis of the internal carotid artery is accompanied by a reduction in wave amplitude from the supraorbital field on that side, whereas the wave amplitude on the contralateral side is little affected. This change is attributed to elimination of flow via the external carotid. Slight slowing of the pulse rate is attributed to the carotid sinus effect.**

fields (figure 3). The wave recorded from the compressed side is noticeably flattened and delayed, which suggests that the blood flow to this supraorbital area is via the external carotid and stenosed internal carotid arteries of the opposite side.

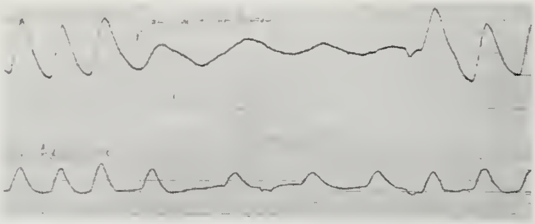

**FIG. 3. Manual compression of the common carotid artery on the contralateral side from stenosis of the internal carotid artery is accompanied by changes in pulse waves from both supraorbital fields. The wave recorded from the compressed side is noticeably flattened and delayed, suggesting that blood flow is via the external carotid and stenosed internal carotid arteries of the opposite side. Reduction in wave amplitude on the noncompressed side was attributed to elimination of the contribution from the external carotid on the compressed side since a previous recording had shown the right superficial temporal artery crossing the midline. Slowing of the pulse rate was attributed to the carotid sinus effect.**

## Conclusions

Photosensor monitoring of the arterial circulation of the skin and subcutaneous tissues in the supraorbital areas by compression of the superficial temporal, angular and occipital arteries provides a method for assessing collateral circulation which may be useful in the detection of carotid artery occlusive disease. Asymmetrical patterns of response to manual compression of the common carotid arteries in the neck have been observed in subjects having unilateral internal carotid artery stenosis. The diagnostic usefulness of the method is under study.

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# Comparison of Selected Scientific and Health Career Choices 1966–1967 versus 1965–1966 of National Merit Scholarship Semi-Finalists*

| Career Choice | Number Selecting in 1965–1966 Program | Number Selecting in 1966–1967 Program | Increase or Decrease |
|---|---|---|---|
| Physician | 791 | 950 | +159 |
| Physicist | 506 | 681 | +175 |
| Scientist (unspecified) | 539 | 480 | −59 |
| Chemist | 288 | 433 | +145 |
| Biological scientist | 266 | 354 | +88 |
| Biochemist | 144 | 237 | +93 |
| Psychologist | 136 | 233 | +97 |
| Social worker | | 97† | |
| Nursing | 100 | 92 | −8 |
| Physical scientist | 83 | 82 | −1 |
| Veterinarian | 42 | 72 | +30 |
| Medical technologist | 60 | 62 | +2 |
| Dentist | 35 | 42 | +7 |
| Pharmacist | 26 | 38 | +12 |
| Biophysicist | 13 | 26 | +13 |
| Physical therapist | 19 | 19 | — |
| Speech therapist | | 6† | |
| Occupational therapist | 5 | 5 | — |
| Physiologist | 4 | 4 | — |
| Health field (unspecified) | | 4† | |
| Grand Totals | 3,057 | 3,917 | +865‡ |
| No. Choosing Other Careers | 6,399 | 7,817 | +1,418 |
| No. Undecided or Unreported | 4,544 | 2,266 | −2,278 |

* Based on an unofficial, noncomputerized tabulation of the career choices shown in the 1966–1967 list of 14,000 National Merit Scholarship Program semi-finalists.

† Not included in tabulation made of 1965–1966 semi-finalists.

‡ Any interpretation of this increase must take into account that 4,544 of the 1965–1966 semi-finalists had either not decided or reported their career choice whereas only 2,266 of the 1966–1967 semi-finalists had not done so.

# Comparison of Results of Brain-scanning with Technetium-99M Pertechnetate and Mercury-197 Chlormerodrin

WILLIAM W. STANBRO, M.D.,* AND CORNELIUS F. MURPHY, M.D.†

WHEN USED FOR BRAIN-SCANNING $^{99m}$Tc pertechnetate has several advantages over $^{197}$Hg chlormerodrin. The most important of these advantages is a higher count rate for a lower radiation dose.

However, the radiation dose from $^{197}$Hg chlormerodrin is within an acceptable range, [1, 2, 3] and by using a low-energy collimator the count rate is increased with resulting improvement in the statistics. In the last analysis a choice between the two will depend primarily upon their relative performance as judged by the diagnostic accuracy of their scans. With this in mind a comparative study is being made of $^{99m}$Tc pertechnetate and $^{197}$Hg chlormerodrin brain scans obtained by scanning each of a group of patients with both isotopes. A comparison of the results obtained in the first 60 patients is the subject of this report.

## Methods

All scans were performed with a Picker Magnascanner having a 5 by 2-inch sodium iodide crystal with a 55-hole low-energy collimator. The low-energy collimator increased the count rate by a factor of 2 over that obtained with a conventional collimator.

The dose of $^{99m}$Tc used for brain-scanning in this study was 5 millicuries. This amount of activity injected intravenously resulted in a maximum of 40,000 to 60,000 counts per minute. Scanning was begun 15 minutes after injection with a scanning speed of 80 to 90 cm. per minute.

The dose of $^{197}$Hg was 15 microcuries per Kg. not exceeding a total dose of 1 millicurie. This amount of activity injected intravenously resulted in a maxiumum of 2,000 to 4,000 counts per minute. Scanning was begun 4 hours after injection with a scanning speed of 38 cm. per minute.

## Results

Twenty of the 60 patients had positive brain scans. In 10 of the 20 both the $^{197}$Hg and $^{99m}$Tc scans were positive and in the remaining 10 only the $^{197}$Hg scans were positive.

Three patients in whom only the $^{197}$Hg scans were positive are not being used in the comparative study because in one the corresponding $^{99m}$Tc scan was technically unsatisfactory and in the other two the positive $^{197}$Hg scans followed the negative $^{99m}$Tc scans after too long an interval. The comparative results in the remaining 17 patients with positive scans are as follows:

Seven patients had positive $^{197}$Hg scans and negative $^{99m}$Tc scans. Two of these results may have been false-positives, and this will be considered in more detail under discussion. Six patients had positive $^{197}$Hg and $^{99m}$Tc scans which were judged to be of equal quality. In 3 patients the $^{197}$Hg scans were superior to the $^{99m}$Tc scans, although both were positive and diagnostic. In 1 patient the $^{99m}$Tc scan was superior to the $^{197}$Hg scan.

## Discussion

In the 7 patients with positive $^{197}$Hg and negative $^{99m}$Tc scans and in the 3 patients in whom the $^{197}$Hg scans were superior to the $^{99m}$Tc scans the interval between scans varied from 1 to 10 days.

Two of the 7 patients with positive $^{197}$Hg and negative $^{99m}$Tc scans may represent false positives in that subsequent arteriograms were negative. Both patients had suffered head trauma, and both were thought to have subdural hematomas. Therefore, it is also possible that the minimal increase in activity noted in the $^{197}$Hg scans was factual and represented traumatic change in the overlying scalp.

Three patients with positive $^{197}$Hg scans and negative $^{99m}$Tc scans had metastatic brain tumors (figure 1, A and B). Two of these were malignant

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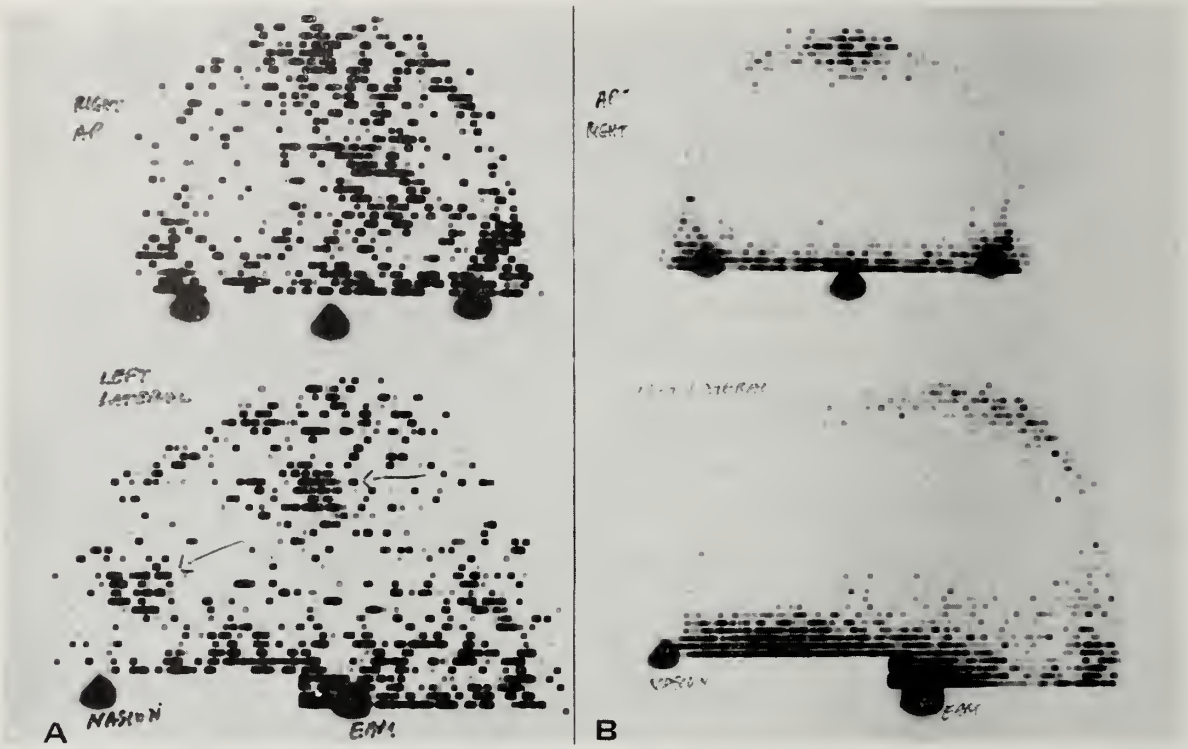
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FIG. 1. A. The $^{197}$Hg scan performed on February 10, 1967 demonstrated 2 metastatic brain tumors. The tumor in the left frontal lobe of the brain was removed at craniotomy and proved to be a malignant melanoma. B. The $^{99m}$Tc scan performed on February 8, 1967 questionably demonstrates a lesion in the frontoparietal area in the left lateral projection but fails to demonstrate the tumor in the left frontal lobe.

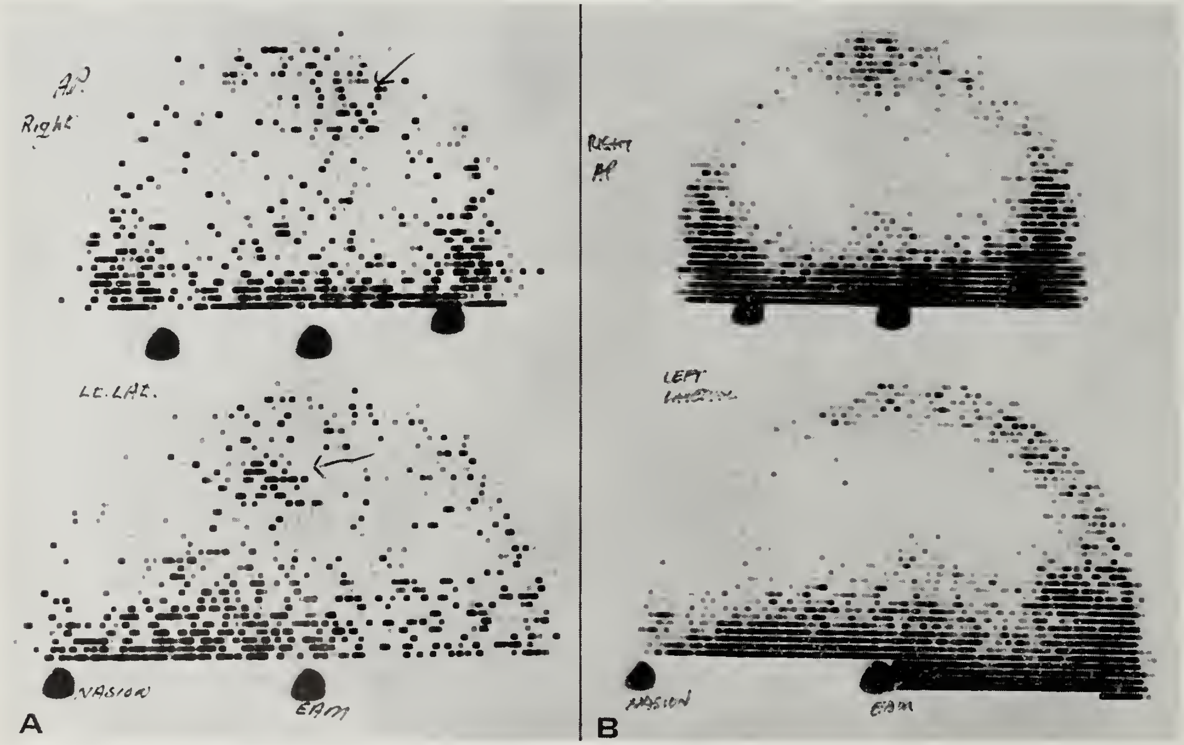
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FIG. 2. A. The $^{197}$Hg scan performed on March 14, 1967 clearly demonstrates a lesion in the posterior portion of the left frontal lobe in a patient with proven bronchogenic carcinoma and clinical evidence of cerebral metastatic disease. B. The $^{99m}$Tc scan performed on March 13, 1967 is at best only questionably positive.

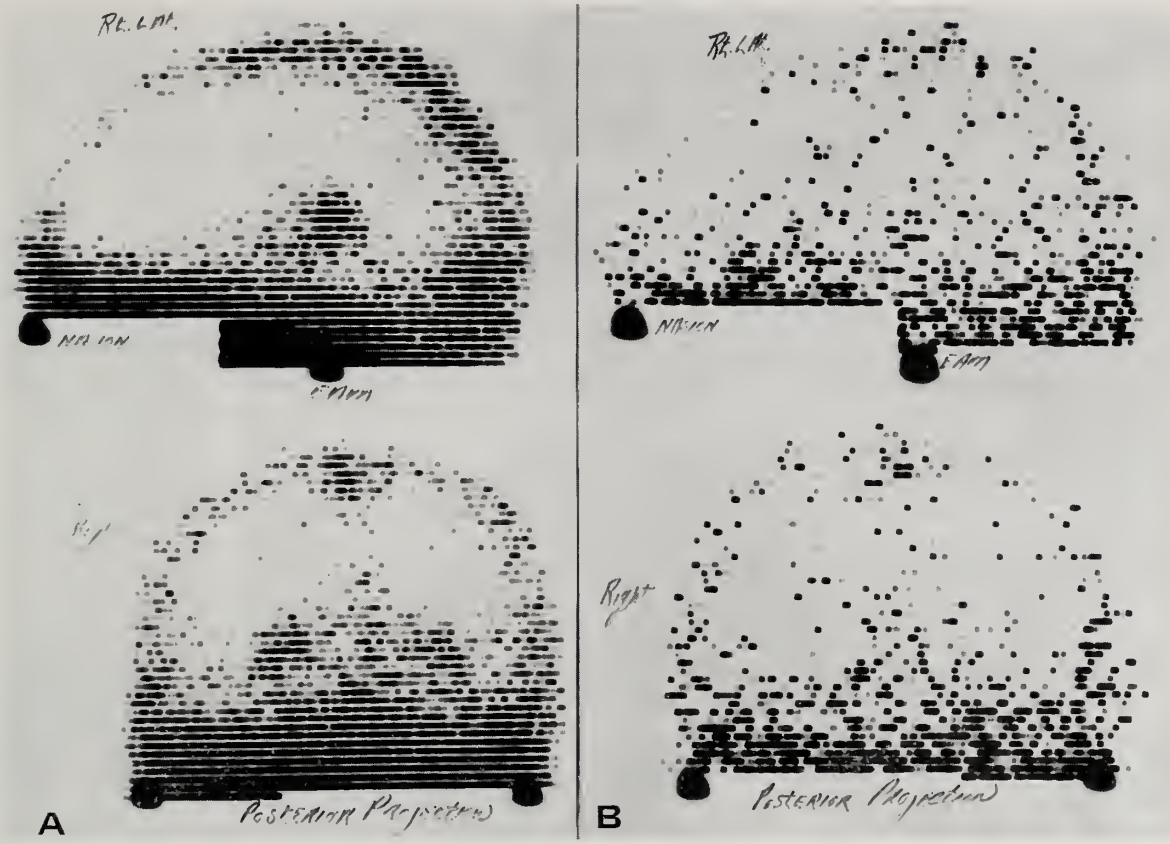

FIG. 3. A. Normal $^{99m}$Tc scan performed on May 1, 1967 demonstrating normal vascular structures. The activity in the region of the choroid plexuses is greater than usual, but some increase in activity is frequently observed in this location, particularly in the lateral projection. B. Normal $^{197}$Hg scan performed on May 2, 1967 demonstrates relatively little activity in the normal vascular structures.

melanomas proved by brain surgery and biopsy, and the third, a patient with inoperable bronchogenic carcinoma proved by thoracotomy and biopsy and who has subsequently developed signs and symptoms of brain tumor, almost certainly has metastases from a lung neoplasm.

One of the patients with positive $^{197}$Hg and negative $^{99m}$Tc scans had a subdural hygroma proved by craniotomy.

One of the patients with positive $^{197}$Hg and negative $^{99m}$Tc scans is thought to have had a vascular accident although it was not proved at surgery.

Of the 3 patients in whom the $^{197}$Hg scans were thought to be superior to the $^{99m}$Tc scans, 2 had primary brain tumors and 1 almost certainly a metastatic brain tumor from a proven lung primary (figure 2, A and B).

The $^{99m}$Tc scans consistently demonstrated normal vascular structures better than the $^{197}$Hg scans (figure 3, A and B). In the $^{99m}$Tc scan (figure 3-A) the increase in activity in the approximate location of the choroid plexuses is more marked than usual, but some increased activity in this area is frequently seen in the lateral projection where it may interfere with the evaluation of the scan.

## Summary

A comparative study of the results of brain-scanning with technetium-99M pertechnetate and mercury-197 chlormerodrin has been made. The comparison of results in 60 patients thus far scanned with both isotopes suggests that $^{197}$Hg chlormerodrin may prove to be superior to $^{99m}$Tc pertechnetate from the standpoint of diagnostic accuracy.

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# Use of Multiple Leads in Fetal Electrocardiography*

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THE FETAL ELECTROCARDIOGRAM (f-ECG) is one of the most useful tools in the diagnosis of fetal life. The earliest f-ECG has been recorded at 11 weeks of gestation.[1] The incidence of positive f-ECGs between 28 and 32 weeks of gestation has been found to be lower than during any other period after the eighteenth week.[1-6] Several explanations of this decreased incidence have been proposed.

The mode of transmission of the fetal signal to the maternal abdominal wall is not well understood. Why the fetal signal can be obtained at some periods of gestation and not at others is difficult to explain. Several investigators have recognized that leads other than the standard midline one are useful to decrease the incidence of false negative tracings. Goodyear et al[7] thought that vertical and diagonal leads are necessary. Multiple abdominal leads have been used by other investigators.[2, 7, 8, 9]

The purpose of this study is to demonstrate that only 1 lead of several available is the best to record the fetal signal in any given case and that such lead cannot be predicted. Therefore, the systematic use of several leads should reduce the number of false negative f-ECGs.

## Material and Methods

Fifty f-ECGs were recorded on 37 pregnant patients from the Obstetrics Clinic at the George Washington University Hospital. The gestational periods of the patients ranged from 11 to 40 weeks; 15 tracings, or 30 per cent, were made on patients between the twenty-eighth and thirty-second weeks of gestation. The following information was obtained from each patient: age, gravidity, parity, number of abortions, number of living and deceased children, last normal menstrual period, and a medical history. No tracings were recorded prior to the eleventh week of gestation or during labor.

The f-ECG was recorded by attaching electrode wires to a grounded Sanborn 55 preamplifier which was then connected to a standard ECG machine. The input signal was amplified 50 times and recorded in the 12- to 20-c.p.s. frequency range. This range filters out most of the baseline interference and gives good fetal QRS complexes. A bipolar lead, with 30 mm. suction cup electrodes, several ground wires, and standard electrode paste were used (figure 1).

The procedure was explained to the patient, and an effort was made to completely relax her. The patient voided prior to the recording. The skin of the anterior abdominal wall was prepared by vigorously rubbing ECG paste at the proposed electrode sites before the electrodes were applied. The f-ECG was recorded with the patient in the dorsal position, arms relaxed at her sides, and legs slightly separated.

Several electrode positions were tried. Anterior-posterior ones, used initially, were discontinued because the tracings obtained were inferior in quality to those obtained from the electrodes on the anterior abdominal wall, and in addition the patients were uncomfortable. Diagonal leads, used in the manner shown in figure 2, produced muscle interference on the tracing; we found that by moving the electrodes closer together we reduced some of the interference and therefore decided to devise a system of electrode placement using short diagonal leads in addition to midline and transverse ones. A total of 6 leads—1 midline, 1 transverse, and 4 diagonals—were used. Electrode locations are shown in figure 3.

Each lead was recorded on heat-sensitive paper at a speed of 25 mm./sec. for a duration of approximately 15 seconds. This provided about 20 maternal cardiac cycles and 50 fetal ones. The best lead or leads were then selected and recorded for a period of 1 minute. According to Lamkee et al[10] a tracing was considered positive if a regular 0.2 to 0.4 second interruption (fetal QRS) of the tracings appeared at a rate independent of the maternal QRS pattern in the tracing and the

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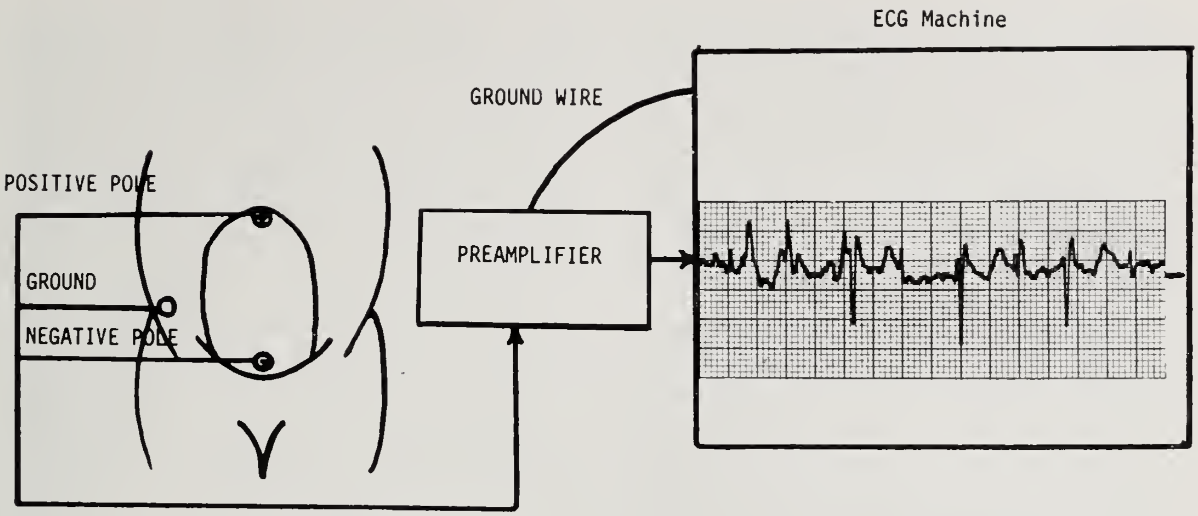

FIG. 1. Diagram of instrumentation.

interruption could be followed thoughout a 15-second portion. The following information was extracted from the tracings: maternal heart rate; fetal heart rate; and relative amplitudes of the fetal QRS complexes, graded from +1 to +4, with 1 the smallest fetal QRS detected, 2 small, 3 medium, and 4 a relatively large amplitude (figure 4). When no fetal signal could be recognized the tracings were graded 0.

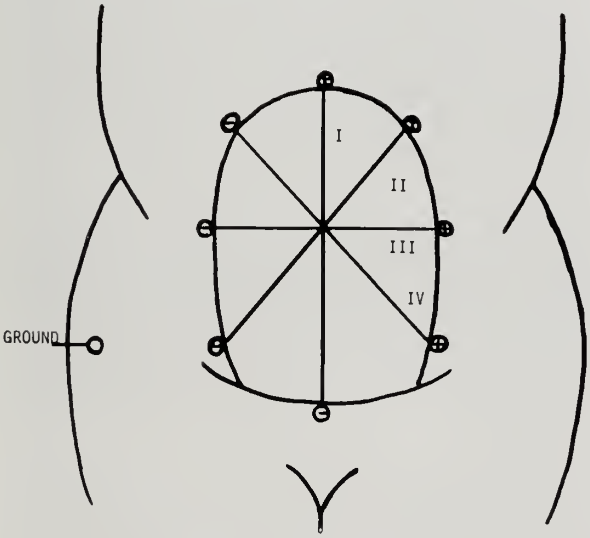

FIG. 2. Electrode positions used initially.

## Results

A positive f-ECG was obtained in 43 tracings (86 per cent). In 7 (14 per cent) no fetal QRS complexes were obtained in any of the 6 leads recorded. In one case fetal demise was clinically suspected when the tracing was recorded; 1 week later this was confirmed by X-ray films. The other 6 f-ECGs are considered false negatives.

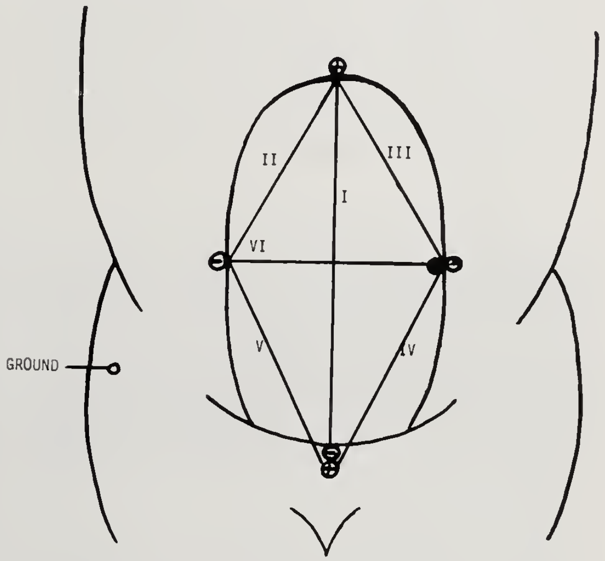

FIG. 3. Sketch of electrode positions:

| | |
|---|---|
| I. Midline lead | Positive pole: fundus<br>Negative pole: symphysis pubis |
| II. Diagonal lead | Positive pole: fundus<br>Negative pole: right middle anterior position |
| III. Diagonal lead | Positive pole: fundus<br>Negative pole: left middle anterior position |
| IV. Diagonal lead | Positive pole: symphysis pubis<br>Negative pole: left middle anterior position |
| V. Diagonal lead | Positive pole: symphysis pubis<br>Negative pole: right middle anterior position |
| VI. Transverse lead | Positive pole: left middle anterior position<br>Negative pole: right middle anterior position |

The maternal heart rates ranged between 67 and 130 beats per minute (average 88). The fetal heart rates ranged between 120 and 170 beats per minute (average 140). The fetal heart rate was considered to be normal in the range of 120 to 160 beats per minute.[11] Below 120 beats per minute fetal bradycardia is present; no cases of bradycardia were observed. A range greater than 160 beats per minute represents fetal tachycardia. Two cases of the latter were observed.

The fetal QRS amplitudes in the 6 leads utilized (I through VI) were graded from 0 to 4 and are presented in table 1. Lead I was the best lead recorded in 23 (46 per cent) tracings. Leads IV and VI were each the best in 5 (10 per cent). Lead V was the best lead in only 2 (4 per cent), and lead II was the best in only 1 (2 per cent). Therefore, in 72 per cent of the tracings only 1 of the 6 leads was the best. In the remaining 14 per cent of positive tracings several combinations of leads were equally good (I and IV in 6 per cent, I and V in 4 per cent, I and VI in 2 per cent, and IV, V and VI in 2 per cent). As mentioned before, no fetal tracing was obtained in the other 14 per cent.

It is also interesting to note the percentage of positive tracings obtained in each lead (table 2). Since the only concern here was to be able to recognize a fetal complex, relative amplitude was not considered. Lead I was positive in 36 (72 per cent) of the tracings. Lead IV was positive in 30 (60 per cent), lead VI in 18 (36 per cent), lead V in 15 (30 per cent), lead III in 10 (20 per cent), and lead II in 7 (14 per cent). Thus a fetal tracing was obtained in lead I most frequently and least in lead II. It is noteworthy that in most cases more than 1 lead was good for obtaining a positive f-ECG. If only 1 lead had been used, from 14 per cent (lead I) to 72 per cent (lead IV) of tracings recorded as positive would have been missed.

## Discussion

One of the major problems in the recording of a positive f-ECG is the low amplitude of the fetal QRS complexes, since it ranges from 10 to 100 microvolts and averages about 40 microvolts.[1] This is very small when compared to the adult range of 1 to 10 millivolts. Other investigators

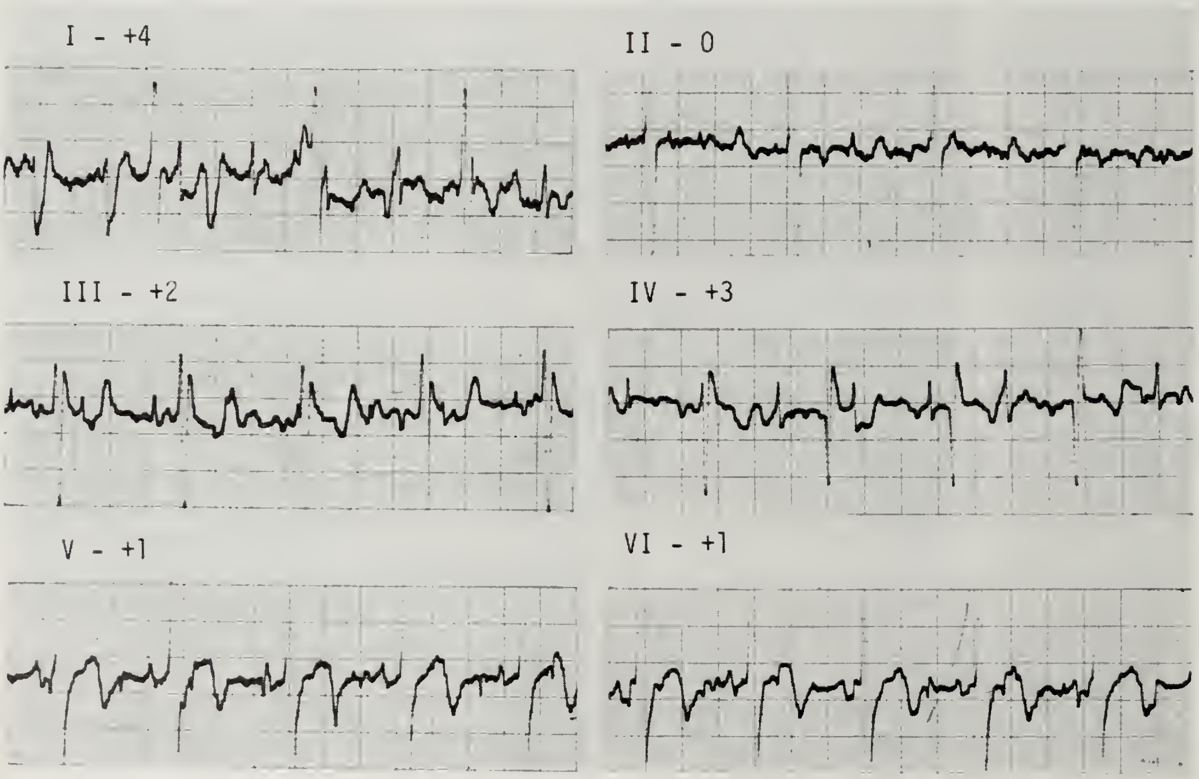

**FIG. 4. Grading of amplitudes in leads I through VI.**
**0—No fetal QRS complex**
**+1—Very small**
**+2—Small**
**+3—Medium**
**+4—Large**

**TABLE 1: Relative Fetal QRS Amplitudes from 0 to +4 in Leads I through VI**

| No. | I | II | III | IV | V | VI | Best Lead(s) | No. | I | II | III | IV | V | VI | Best Lead(s) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | +4 | +2 | +2 | +3 | +4 | +1 | I, V | 26 | +4 | +3 | +3 | +3 | +1 | +3 | I |
| 2 | +3 | 0 | 0 | 0 | 0 | 0 | I | 27 | +2 | 0 | 0 | 0 | 0 | 0 | I |
| 3 | +1 | 0 | 0 | +3 | 0 | 0 | IV | 28 | +4 | 0 | 0 | +3 | +2 | 0 | I |
| 4 | +4 | 0 | 0 | +3 | 0 | 0 | I | 29 | +1 | 0 | 0 | +2 | 0 | 0 | IV |
| 5 | +1 | 0 | 0 | 0 | +2 | +4 | VI | 30 | 0 | 0 | 0 | +3 | 0 | 0 | IV |
| 6 | +2 | 0 | 0 | +1 | 0 | 0 | I | 31 | +3 | 0 | 0 | +2 | 0 | +2 | I |
| 7 | +3 | +1 | +2 | 0 | 0 | +4 | VI | 32 | +4 | 0 | +3 | 0 | +2 | 0 | I |
| 8 | +4 | 0 | 0 | +3 | 0 | 0 | I | 33 | +3 | 0 | 0 | +1 | +3 | +2 | I, V |
| 9 | 0 | 0 | 0 | +3 | +4 | 0 | V | 34 | 0 | 0 | 0 | 0 | 0 | 0 | * |
| 10 | +3 | 0 | 0 | +2 | 0 | 0 | I | 35 | +3 | 0 | 0 | +2 | 0 | +3 | I, VI |
| 11 | 0 | +1 | 0 | +3 | 0 | +4 | VI | 36 | 0 | +3 | 0 | +2 | 0 | +1 | II |
| 12 | +4 | 0 | +3 | 0 | 0 | 0 | I | 37 | +4 | +1 | +3 | +4 | +3 | +3 | I, IV |
| 13 | +4 | 0 | 0 | +3 | 0 | 0 | I | 38 | 0 | 0 | 0 | 0 | 0 | 0 | * |
| 14 | +4 | 0 | +2 | +4 | 0 | +3 | I, IV | 39 | 0 | 0 | 0 | +1 | 0 | +3 | VI |
| 15 | +4 | 0 | +2 | +3 | +1 | +1 | I | 40 | +3 | 0 | 0 | 0 | +2 | +1 | I |
| 16 | +2 | 0 | +2 | +4 | +4 | +4 | IV, V, VI | 41 | +3 | 0 | 0 | 0 | 0 | 0 | I |
| 17 | +1 | 0 | 0 | 0 | 0 | 0 | I | 42 | +1 | 0 | 0 | +2 | 0 | +3 | VI |
| 18 | +3 | 0 | 0 | +3 | +2 | 0 | I, IV | 43 | +3 | 0 | 0 | +2 | 0 | 0 | I |
| 19 | 0 | 0 | 0 | 0 | 0 | 0 | * | 44 | +2 | +1 | 0 | 0 | 0 | 0 | I |
| 20 | 0 | 0 | 0 | 0 | 0 | 0 | * | 45 | 0 | 0 | 0 | +3 | 0 | 0 | IV |
| 21 | 0 | 0 | 0 | 0 | 0 | 0 | * | 46 | +2 | 0 | 0 | +1 | 0 | 0 | I |
| 22 | +3 | 0 | 0 | 0 | 0 | 0 | I | 47 | +4 | 0 | +3 | +2 | +3 | +1 | I |
| 23 | +3 | 0 | 0 | 0 | +1 | 0 | I | 48 | 0 | 0 | 0 | 0 | 0 | 0 | * |
| 24 | +4 | 0 | 0 | +3 | 0 | +2 | I | 49 | 0 | 0 | 0 | 0 | 0 | 0 | * |
| 25 | 0 | 0 | 0 | +2 | 0 | 0 | IV | 50 | 0 | 0 | 0 | 0 | +2 | 0 | V |

* Negative fetal tracing.

have found that the fetal R wave averages about 25 microvolts in amplitude. A sensitivity of 100 times of that required for the adult ECG is necessary to get a comparable fetal tracing. Therefore equipment other than a standard ECG machine is required. Even with sensitive instruments fetal P and T waves and ST segments are still rarely obtained. Only a few investigators have been able to obtain the latter. Intravaginal and intrauterine electrodes have been the most effective for this purpose.[12, 13] These techniques are obviously too cumbersome for routine clinical use.

Understanding the pathway of transmission of the fetal signal to the maternal abdominal wall might help in explaining why a f-ECG is positive at one time and negative at others. This pathway is presently not well understood. Larks[1] believes that the fetal signal is transmitted from its source through a simple volume conductor to the maternal skin surface in a manner similar to that in the adult or infant. It has recently been postulated[14] that the nasopharyngeal and umbilical cord areas are of low impedance (as compared to the rest of the fetal skin) through which the fetal signal is easily transmitted. This low impedance pathway of transmission theory is also supported by Roche and Hon[9]; however, they could not explain some of their observations. As a possibility they suggested that the various changes in fetal position in utero might explain why the signal varies during pregnancy.

**TABLE 2: Percentage of Positive and Negative Tracings with a Single Lead as Opposed to the 6 Leads**

| Lead | Positive Tracings | | Negative Tracings | | Tracings Which Became + After the Use of Other Leads | |
|---|---|---|---|---|---|---|
| | No. | Per cent | No. | Per cent | No. | Per cent |
| I | 36 | 72 | 14 | 28 | 7 | 14 |
| II | 7 | 14 | 43 | 86 | 36 | 72 |
| III | 10 | 20 | 40 | 80 | 33 | 66 |
| IV | 30 | 60 | 20 | 40 | 13 | 26 |
| V | 15 | 30 | 35 | 70 | 28 | 56 |
| VI | 18 | 36 | 32 | 64 | 25 | 50 |

We believe that a likely explanation of some of the negative tracings recorded is that the optimal lead was not used. Ward and Kennedy[15] used 3 abdominal leads which formed an equilateral triangle over the uterus with the apex at the fundus; they found that the fetal waves usually appear in only 1 lead. No statistical evaluation was provided in that report. Bergman and Hall,[2] using a flank-to-flank lead in the umbilical plane in addition to the symphysis-to-fundus one, believed that the frequency of positive tracings was increased by the use of several leads. This finding is supported by our study. Roche and Hon,[9] with a detailed mapping system in the placement of electrodes in order to locate the area of maximum fetal amplitude, found that in 95 per cent of the cases the amplitude of the fetal QRS complex was maximum in an area adjacent to and above the umbilicus between the anterior axillary lines. Others, using multiple abdominal leads, have concluded that the midline one was superior.[10, 16] In spite of using multiple abdominal leads, most of the investigators have reported a decreased incidence of positive tracings during certain periods of gestation, mainly the twenty-eighth to thirty-second weeks. In most of the studies reporting a low incidence of f-ECGs recorded during the 28–32 week period only 1 preselected lead was used.

Several factors have been postulated to explain why positive tracings are not obtained on occasion: (1) an increase in vernix caseosa[6]; (2) changes in the amount and composition of the amniotic fluid[1]; (3) changes in the overlying tissues[1]; and (4) changes in fetal orientation.[9, 14]

It is difficult to make a general statement about the percentage of positive tracings that various investigators have obtained, since it varies with the instrumentation used, lead placement, and period of gestation. Using a midline lead alone, Larks[1] found positive fetal tracings in 40 per cent of his patients before 18 weeks of gestation, 97 per cent from 18-24 weeks, 75 to 80 per cent between 24 and 32 weeks with a low of 50 per cent at 31 weeks, and 97 per cent from 32 weeks to term. Using the same lead, Hsu and Buxton[17] reported an overall incidence of 89.5 per cent between 18 and 41 weeks of gestation. With multiple abdominal leads various incidences of positive results have been obtained: (1) Paley and Krell[16] reported 79 per cent in patients in the fifth to ninth months of gestation; (2) Bernstein and Mann[3] reported 79.8 per cent in the fourth to tenth lunar months; (3) Hon and Hess[18] reported 88 per cent in patients between the sixteenth and twentieth weeks, and 78 per cent from 20 weeks to term; (4) Lamkee et al[10] reported an overall incidence of 88 per cent between 12 weeks and term; and (5) Ward and Kennedy[15] one of 67 per cent between 7 and 40 weeks and 82 per cent between 16 weeks and term.

The most important uses of fetal electrocardiography are for the detection of fetal life and the diagnosis of multiple pregnancy. The earliest recording of a multiple pregnancy was made by Mattingly[4] at 12 weeks of gestation. The clinical significance of the early diagnosis and obstetrical management of multiple pregnancy has been summarized by Barter et al.[19] The analysis and study of the fetal QRS morphology or pattern can provide information in regard to fetal presentation as shown by Strassman and others.[1,4, 20] The fetal heart rate has been used frequently for the detection and evaluation of fetal distress or anoxia. It has been found that tachycardia is frequently associated with fetal distress.[21] Bradycardia is often transient and related to uterine contractions during labor and is of little significance. However, if it persists more than 48 seconds or continues during the intercontraction periods, fetal anoxia must be considered.[1, 22] In a few studies fetal abnormalities have been suspected on the basis of an abnormal f-ECG.[1, 23]

## Summary and Conclusions

The fetal electrocardiogram (f-ECG) is a useful tool in diagnosing fetal life. During certain periods of gestation a positive tracing is more difficult to record than during others. It is particularly difficult during the 28–32 week period. Various factors have been postulated to explain the failure to obtain positive tracings.

A major problem in recording a fetal tracing is the low amplitude of the fetal QRS complex. How the fetal signal is transmitted to the maternal skin surface is not well understood; we do not know why a tracing is frequently negative in spite of the presence of fetal life. Some investigators have found that multiple leads increase the incidence of positive tracings while others think that it is only necessary to record a midline lead.

This study was undertaken to evaluate whether the use of several leads in all cases would increase the number of positive tracings.

Fifty f-ECGs were recorded on 37 pregnant patients ranging from 11 to 40 weeks of gestation; 15 (30 per cent) tracings were obtained during the 28–32 week period. The f-ECGs were recorded from the maternal abdominal wall. Six leads were used (1 midline, 1 transverse and 4 diagonal).

Positive tracings were obtained in 43 (86 per cent). One of the 6 leads was the best in 72 per cent of the tracings. In the remaining 14 per cent of positive tracings several leads were equally good. A fetal tracing was obtained most frequently in lead I (36 tracings, 72 per cent) and least in lead II (7 tracings, 14 per cent).

If, instead of using 6 leads as in our study only 1 lead had been used, from 14 per cent (lead I) to 72 per cent (lead II) of tracings recorded as positive would have been missed.

This study suggests the following conclusions: (1) When several leads are recorded 1 lead is generally the best for recording an f-ECG; (2) if only 1 lead is used we have a lower percentage of positive tracings; and (3) a possible explanation for a decreased incidence of positive tracings during certain periods of gestation would be that the optimal lead was not used.

Thus, in recording f-ECGs, we recommend using several leads. The technician should try all of them for a few seconds, then record about 1 minute (or whatever time is desired)on the lead that shows the best fetal QRS complex. This routine practice would decrease the incidence of negative f-ECGs.

Thanks are due to Drs. Cecil Jacobson and Richard Erkenbeck of the Department of Obstetrics and to Dr. Irene Hsu of the Department of Cardiology for their coöperation in this study. Mrs. Josephine McFadden assisted in the recording of the tracings. Miss Anne Lush' help is also appreciated.

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## Plan for Outpatient Veteran to Choose Own Doctor

A new program to reduce costs and improve service in outpatient care is being inaugurated by the Veterans Administration following a successful test program in 3 states.

Since World War II the Veterans Administration has authorized outpatient care by private doctors, at Government expense, for certain qualified veterans. Most of these patients have service-connected disabilities. Hometown medical care is authorized in such cases when treatment at a VA medical facility would involve a long trip or other hardship. Under the old rules VA estimated how much care each such veteran would need during the coming year and issued an authorization to a specific doctor to give treatment at Government expense.

Under the new program VA will issue an identification card to veterans who require this type of treatment, and each patient will be permitted to select a doctor of his choice for treatment of the medical condition stated on his card.

Tests of the new system—conducted in Indiana, Colorado and Alabama—demonstrated that administrative costs of providing this treatment were reduced significantly.

Both the patient and the doctor also benefit by the new plan. The patient can visit the doctor of his choice as often as his doctor considers necessary. The doctor is relieved of much of the paper work associated with the old system. Instead of preparing a medical report and a claim form he merely files an itemized bill on his own letterhead just as he does for his other patients. Medical reports to the VA are filed by the doctor only when there is a significant change in the veteran's service-connected condition.

In the 3-state test program conducted by VA before the system was adopted Nationwide, both veterans and doctors coöperated with the program. Doctors provided care consistent with sound judgment and ethical medical practice, and there was no evidence that veterans abused the greater freedom of choice and the reduced controls. In fact, there was a slight decrease in the average number of visits per veteran.

# Familial Neutropenia

## Report of Six Cases in One Family

EDWARD J. FEROLI, M.D.*

THIS REPORT of familial neutropenia involving 6 members of a family is presented because of the rarity with which this disease has been reported, especially in the American literature. Familial neutropenia is one of several names applied to a chronic benign granulocytopenia with a genetic predisposition. This terminology was introduced by Bousser and Neyde[1] in 1947. An earlier nomenclature was familial constitutional neutropenia, used by Gänsslen[2] in 1941 to describe the first cases reported. Typically, this disease is characterized by neutropenia, leukopenia, frequently an increased susceptibility to infection, occasionally spontaneous remissions, and a bone marrow that may be normal or may show maturation arrest at the myelocyte level.[3]

### Report of Cases

**Case 1.** R. R., the index case, was a 10-month-old white female admitted to William Beaumont Army Hospital on August 20, 1962 for evaluation of motor retardation. She had an uncomplicated prenatal and neonatal history. Her birth weight was 6 lbs., 15 oz. At 5 months of age she had crying spells with stiffening of her extremities. At 6 months of age she had a smallpox vaccination with a primary "take." At 10 months of age she could not roll over, sit or laugh. There was no history of drug ingestion or unusual susceptibility to infection.

The baby was well-nourished, obviously retarded, and had normal vital signs. Her weight was 20 lbs., her length 28½ inches, and her head circumference 16¼ inches (less than the 3 percentile). She did not socialize, and her motor ability was greatly retarded. The fundi were normal. There was no splenomegaly or evidence of infection. Laboratory studies including urinalysis, urine amino acids, chest X-ray film, skull X-ray films, long bone survey, PBI, toxoplasmosis complement fixation, and EEG were all normal. The initial white blood cell count was 11,000 with 3 per cent neutrophils, 87 per cent lymphocytes, 5 per cent monocytes, and 5 per cent eosinophils. The hematocrit was 45. The diagnosis was primary microcephaly and neutropenia of unknown etiology.

At 11 months of age the baby began having generalized seizures which were initially controlled with phenobarbital but later required the addition of Dilantin®. At 12 months of age she developed a small abscess on her forehead without systemic symptoms. This was incised and drained, and a culture revealed *Hemolytic staphylococcus aureus.* She was given 2 injections of procaine penicillin of 300,000 units each, and the infection rapidly resolved. At 14 months of age she had acute coryza which resolved on symptomatic therapy after a neutrophil rise to 21 per cent. Further laboratory tests performed at 16 months of age showed negative tests for syphilis, lupus preparations, and direct and indirect Coombs' tests. The leukocyte alkaline phosphatase level was 20 units (normal is 20–100 U.). Serum electrophoresis revealed a total protein of 7.9 Gm. with albumin 78.0, alpha-1-globulin 2.7 Gm., alpha-2-globulin 4.7 Gm., beta globulin 9.3 Gm., and gamma globulin 5.3 Gm. (419 mg. per cent). A bone marrow smear disclosed "blasts" 3.5 per cent, promyelocytes 5 per cent, myeloneutrophils 13 per cent, myelo-eosinophils 1 per cent, myelobasophils 0.5 per cent, metamyelocytic neutrophils 28 per cent, metamyelocytic eosinophils 0.5 per cent, metamyelocytic basophils 0.5 per cent, polymorphonuclear neutrophils 15 per cent, polymorphonuclear eosinophils 2 per cent, lymphocytes 7 per cent, plasma cells 1 per cent, pronormoblasts 4.5 per cent, basophilic normoblasts 8 per cent, polychromatophilic normoblasts 10 per cent. The M.E. ratio was 2.7/1. Some of the myelocytes were large and atypical. The ACTH white blood cell stimulation test[4] was normal. This is performed by counting white blood cells before and at 2-hour intervals after the injection of 15 mg. ACTH as shown below:

| | WBC | N | L | E | M | Bands | N/ cu.mm. |
|---|---|---|---|---|---|---|---|
| Injection time..... | 12,000 | 9 | 86 | 3 | 2 | | 1,080 |
| 2 hours after injection.......... | 6,700 | 36 | 61 | 3 | | | 2,412 |
| 4 hours after injection.......... | 8,200 | 39 | 59 | 1 | | 1 | 2,598 |

(The 141 per cent increase in neutrophils is a normal response.)

The epinephrine white blood cell stimulation test[5] was also normal. This may be performed by counting white blood cells before and at 15-minute intervals after a subcutaneous injection of 0.2 ml. epinephrine 1:1,000. A rise in neutrophil count is anticipated as follows:

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* Office: 11125 Rockville Pike, Rockville, Md. 20852.

| | WBC | N | L | E | B | N/ cu.mm. |
|---|---|---|---|---|---|---|
| Injection time | 5,000 | 4.8 | 88.6 | 6.2 | 0.4 | 240 |
| 15 minutes after injection | 12,000 | 6.0 | 88.4 | 4.6 | 0.2 | 720 |
| 20 minutes after injection | 9,800 | 6.2 | 91.0 | 2.6 | 0.2 | 608 |

(All counts were based on 500 white cells counted. The 200 per cent increase in neutrophils per cu. mm. represents a normal response.)

For a review of all white blood cell counts see table 1.

**TABLE 1: Random White Blood Cell Counts in the R Family, the Maternal Grandparents, Mr. and Mrs. Y, and the Maternal Uncle, W. Y.**

| | Date | WBC | N | E | B | L | M | Bands | N/cu.mm.* | Complications |
|---|---|---|---|---|---|---|---|---|---|---|
| R. R. | 8-20-62 | 11,000 | 3 | 5 | 0 | 87 | 5 | | 330 | |
| | 8-23-62 | 7,200 | 5 | 2 | 0 | 90 | 3 | | 360 | |
| | 8-28-62 | 5,100 | 7 | 1 | 0 | 87 | 5 | | 357 | |
| | 10-8-62 | 8,200 | 5 | 7 | 0 | 88 | 0 | | 410 | Small abscess—*Staph. aureus* |
| | 11-7-62 | 6,400 | 6 | 4 | 0 | 87 | 3 | | 384 | |
| | 11-19-62 | 10,800 | 7 | — | — | 93 | — | | 756 | |
| | 11-26-62 | 8,700 | 10 | 1 | — | 88 | 1 | | 870 | |
| | 12-10-62 | 8,800 | 10 | — | — | 87 | 1 | 2 | 880 | Coryza |
| | 12-13-62 | 10,900 | 21 | — | — | 75 | 4 | Plate—N | 2,289 | Coryza |
| | 2-14-63 | 6,400 | 1 | 2 | — | 97 | | Plate—N | 64 | Resolving coryza |
| | 5-20-63 | 8,100 | 5 | 2 | 1 | 92 | | | 405 | Furuncles |
| | 6-17-63 | 6,000 | 10 | | | 90 | | | 600 | |
| W. Y. | 7-12-63 | 6,500 | 21 | 1 | | 78 | | | 1,365 | |
| | 7-13-63 | 6,100 | 24 | | | 76 | | | 1,464 | |
| Mr. Y | 4-23-63 | 5,000 | 26 | 3 | 1 | 69 | | 1 | 1,300 | |
| Mrs. Y | 4-23-63 | 9,800 | 54 | 4 | 1 | 40 | | 1 | 5,292 | |
| Mrs. R | 8-28-62 | 5,800 | 35 | 4 | | 58 | 3 | | 2,030 | |
| | 5-20-63 | 5,100 | 15 | 4 | | 81 | | | 765 | |
| K. R. | 10-15-62 | 11,100 | 60 | 2 | | 27 | 9 | 2 | 6,660 | (born 10-14-62) |
| | 11-1-62 | 7,500 | 35 | 2 | | 59 | 4 | | 2,625 | |
| | 2-14-63 | 8,200 | 12 | 5 | | 83 | | Plate—N | 984 | |
| | 5-20-63 | 8,000 | 9 | 3 | 1 | 87 | | | 720 | |
| M. R. | 8-28-62 | 5,400 | 10 | 2 | | 87 | 1 | | 540 | |
| | 5-20-63 | 5,300 | 30 | 3 | | 67 | | | 1,620 | |
| Mr. R | 8-28-62 | 5,700 | 59 | 1 | | 38 | 2 | | 3,363 | |

* Number of neutrophils per cu. mm.

**Case 2.** Mrs. R., the mother of R. R., had been told several times that she had "low white blood cells." She was 32 years old, of German-Irish-Austrian descent, and was never troubled by serious or frequent infections nor was she on drug therapy. A complete blood count revealed neutropenia. Serum electrophoresis showed total protein 6.9 Gm., albumin 69.0 Gm., alpha-1-globulin 2.6 Gm., alpha-2-globulin 3.2 Gm., beta globulin 14.2 Gm., and gamma globulin 11.0 Gm. (759 mg. per cent). Leukocyte alkaline phosphatase was 30 U. A bone marrow smear was interpreted as normal.

**Case 3.** M. R., the 5-year-old brother of R. R., had never had recurrent or serious infections. The leukocyte alkaline phosphatase level was 32 U.

**Case 4.** K. R. is a sister born on October 14, 1962 when R. R. was 1 year old. At 1 day of age she had a white blood cell count of 11,100 with 60 per cent neutrophils. This percentage subsequently declined to neutropenic levels. Her leukocyte alkaline phosphatase level was 48 U. At the present writing she is 10 months old and has shown no increased incidence of infection.

**Case 5.** Mr. Y., the maternal grandfather of R. R., is 62 years old and of Austrian-German descent. He had worked in coal mines for 30 years and was diagnosed as having silicosis in 1958. He has had no history of serious or frequent infections.

**Case 6.** W. Y., the maternal uncle of R. R., is a single 38-year-old factory worker with no history of serious illness.

Two other people should be considered:

Mr. R., the father of R. R., is a 37-year-old Army sergeant of Irish descent who has always had satisfactory health and has a normal white blood cell count.

Mrs. Y., the maternal grandmother of R. R., is a 58-year-old woman of German-Irish descent who had pneumonia at 8 years of age but had no other serious infections in the past. However, 3 years ago she was felt to have bronchiectasis and presently has a chronic cough with daily temperatures ranging from 99 to 101°F. She is robust and healthy in appearance. Her blood studies reveal a white blood cell count of 9,800, with neutrophils 54 per cent, bands 1 per cent, eosinophils 4 per cent, lymphocytes 40 per cent, and monocytes 1 per cent. With her present infection it is difficult to determine whether or not she has neutropenia, and thus she cannot be considered in this category.

## Discussion

Historically, numerous reports of chronic benign granulocytopenia (nonfamilial) are found in the literature.[6-10] This disease or condition is quite variable as to symptoms and laboratory findings. The neutrophil percentage may vary from less than 1 per cent to near normal. The neutrophil count may or may not increase with infection. There is usually leukopenia but occasionally a normal white blood cell count. The bone marrow may be normal or show maturation arrest at the myelocyte stage. Clinically it varies from complete lack of symptoms to death from infection despite antibiotic therapy. There may be persistent chronicity or spontaneous remission after months or years. The typical course is that of recurring infections of the skin and oral mucous membranes with associated fever.

There is little available in the literature if the discussion of chronic benign granulocytopenia is limited to the genetic or familial type. The first report was by Gänsslen[2] in 1941 entitled "Constitutional Familial Leukopenia." Four families with this trait were detected in a white blood cell count survey of several thousand individuals in Frankfurt, Germany. All families studied showed similar characteristics: neutrophil percentage from 34 to 65, absolute neutrophil count from 777 to near normal, and white blood cell count between 2,100 and 5,300. Clinically all were asymptomatic. The largest family described involved an affected grandfather, 2 of his 7 children, and 4 of the 6 grandchildren. Gänsslen claimed that this represented autosomal dominant inheritance. No bone marrow studies were reported.

It is interesting that the R family also has a strong Germanic background; the maternal grandmother is German-Irish, and the maternal grandfather is of German-Austrian descent. Since 4 families with familial neutropenia were discovered in the Frankfurt area alone, one wonders whether this might not be a geographic haven for this condition in light of its universal rareness. Also the character of the disease in the 4 families is remarkably consistent. These cases differ from the R family in that the families in Frankfurt had a generally higher neutrophil percentage and a persistent leukopenia.

Bousser and Neyde[1] described 2 cases of familial neutropenia which occurred in a 24-year-old man and his mother. Both were asymptomatic. In these cases the total white blood cell count ranged from 2,000 to 3,500 and neutrophils from 35 to 50 per cent (700 to 2,500/cu. mm.). Monocytes ranged from 7 to 16 per cent but were normal in absolute count. An injection of adrenalin tended to normalize the leukocyte count. The bone marrows were interpreted as showing myeloid hypoplasia.

Infantile genetic agranulocytosis was described by Kostmann.[11] This disease was found to afflict many generations of a family living in a sharply localized area in northern Sweden. The case histories of 14 affected children were described. Typically skin infections began in early infancy with death from septicemia or pneumonia occurring a few weeks to months later. The total white blood cell counts were usually normal or elevated while the neutrophils were often less than 1 per cent (absolute count less than 100 per cu. mm.). The monocyte counts were usually elevated, ranging up to 70 per cent. It was believed that the monocytes functioned as phagocytes to compensate for the decreased neutrophils. Two children were 4 years of age at the time of the writing. They had normal total white blood cell counts with 4 to 35 per cent neutrophils and a normal monocyte percentage. Bone marrows were studied in 4 children, and in all instances there was a maturation arrest at the myelocyte stage. The author concluded that this disease was inherited as a single recessive autosomal gene. He also stated that this was a lethal gene and mentioned that the 2 surviving 4-year-olds were doomed to an early death which had been postponed only through the use of antibiotics. These 2 children, however, had higher neutrophil counts than the others. These levels when compared with reported cases of benign granulocytopenia were not at all inconsistent with a normal lifespan.

Bjure, Nilsson, and Plum[12] reported 2 brothers with familial neutropenia who were symptomatic since infancy. Bone marrow studies revealed maturation arrest at the myelocyte level. In vitro bone marrow culture experiments suggested that the serum from these brothers tended to inhibit the growth activity of normal bone marrow. When the brothers were transfused with fresh plasma from normal donors, myelopoiesis was normalized in one with a questionable effect in the other. This report concluded that neutropenia might be caused by a deficiency of a plasma factor.

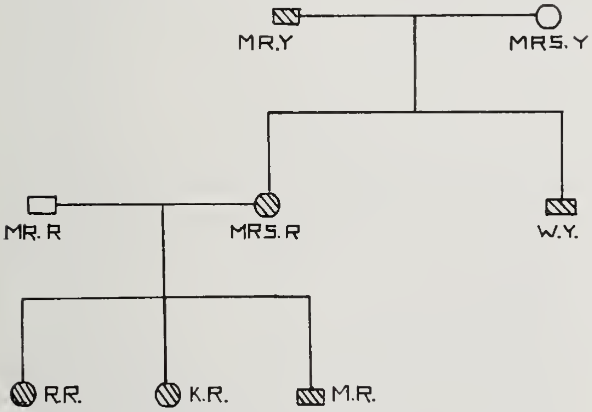

**FIG. 1. Inheritance of neutropenia in the R family. The shaded symbols represent the affected members.**

Figure 1 shows the distribution of the neutropenia in the R family which was probably inherited as an autosomal dominant trait.

Neutropenia is usually defined as a neutrophil count less than 2,500 per cu. mm.[13] Leukopenia is a total white blood cell count less than 4,000. The course in all of our patients has been truly benign, unlike most previously reported cases where recurrent infections play a prominent part. DeGruchy[13] believes that the point at which neutropenia per se causes symptoms varies from patient to patient: When the neutrophil count is between 1,500 and 2,500/cu. mm. symptoms are uncommon; from 500 to 1,500/cu. mm. symptoms may or may not occur; and when a count is below 500/cu. mm. clinical manifestations are common and often severe. The affected members of this family, except R. R., belong to the 500 to 1,500 neutrophil group. R. R. often has a neutrophil count less than 500 but has mild infrequent infections. It should be appreciated that the presence of neutrophils in the bloodstream is a transient affair in the life of these white blood cells.[14] Approximately 12 days are spent in formation and maturation, 9 hours in circulation and an indeterminate time in the tissues. Thus, some authors deny that neutrophils should be called white blood cells but would consider them bone marrow cells which pass through the bloodstream en route to tissues. Hence bone marrow and tissue levels may be more important than blood levels per se, although the 3 may fluctuate in like manner.

The normal response of R. R. to the ACTH stimulation test[4] could probably have been predicted since her neutrophils had risen to 21 per cent in response to an upper respiratory infection. ACTH and bacterial toxins stimulate an outpouring of granulocytes from the bone marrows of normal subjects. Since it is estimated that there are 25 to 30 times as many granulocytes in the normal marrow as in the general circulation, it is evident that there is a large granulocyte pool in reserve. The increased bone marrow release of neutrophils after ACTH injection in R. R. is thus a partial measure of her resistance and is reflected by her clinical course. Although the maximum neutrophil level obtained was only 39 per cent, this is considerably better than would occur in a patient with cyclic neutropenia,[15] in which condition the patient may obtain symptomatic relief from ACTH but the neutrophil count is not significantly affected.

An increase in neutrophils and leukocytes in response to epinephrine is an entirely different phenomenon.[5] It has been shown that the leukocytes may circulate freely in the blood, adhere to the vascular endothelium in the sites where blood flow is relatively slow, and then once again reënter the circulation in a process of continual exchange. The granulocytes which are attached to the blood vessel walls are called marginated. The granulocytes are thus distributed in a pool of cells larger than that which could be calculated from the blood volume and concentration of granulocytes in the circulating blood. In past studies, after radioactive-labeled granulocytes were injected into a human host, only 50 per cent could be recovered. After epinephrine infusion 77 to 88 per cent of the labeled granulocytes could be recovered, and after vigorous exercise 54 to 100 per cent could be found. It was calculated that the marginated pool of granulocytes is approximately equal to the number of circulating granulocytes. It is believed that exercise and epinephrine may mobilize marginated cells simply by increasing blood flow. The normal response to epinephrine seen in R. R. rules out a defect in the release of marginated granulocytes and suggests that the pools are of equal size, as expected.

*(Continued on page 750)*

# Bilateral Polycystic Ovaries with a Dermoid Cyst of One Ovary

DAVID H. KUSHNER, M.D., F.A.C.O.G., F.A.C.S.,* AND JAI YEOUNG AHN, M.D.†

In 1935 Stein and Leventhal[1] reported a series of 7 patients in which amenorrhea was associated with bilateral polycystic ovaries. Wedge resection of the ovaries successfully restored their physiologic function. Since the initial description many publications have accumulated in the literature confirming these original observations. This entity is now being recognized more frequently as the physician's index of suspicion increases.[2]

In the collective review of published cases by Goldzieher and Green[3] in 1962 there is no mention concerning polycystic ovaries in association with dermoid cyst of the ovary. On the other hand, several excellent studies on dermoid cyst of the ovary[4, 5, 6] revealed no instances in which these 2 pathologic entities were present in the same patient. The following report concerns such a patient.

## Report of Case

A 15-year-old white girl was first seen on December 3, 1962 with the chief complaint of delayed menarche. The past history was noncontributory. Physical examination including rectal examination revealed no abnormalities. The patient had no stigmata of endocrinopathy and possessed normal secondary sex characteristics. An attempt to elicit uterine bleeding by the use of 100 mg. of aqueous progesterone (Lipo-Lutin Aqueous®) failed. On December 18, 1962 she was given estradiol valerate (Delestrogen®) 20 mg. followed 2 weeks later by hydroxyprogesterone caproate (Delalutin®) 500 mg. She experienced uterine bleeding for the first time. The patient was not seen again until August 30, 1963, at which time she said she had not menstruated since the induced uterine bleeding. The patient was again placed on cyclic therapy with the administration of conjugated estrogenic substance (Premarin®) 1.25 mg. for 20 consecutive days followed by hydroxyprogesterone caproate (Delalutin) 500 mg. This therapy induced uterine bleeding. Menstruation occurred in the next several months while she was on repeated cyclic hormone therapy. Spontaneous menstruation failed to occur and she was given methylprednisolone (Medrol®) 8 mg. orally daily for a period of 60 days with no result. She was seen on January 2, 1965 at the age of 17½ years. She had not menstruated since the previous cyclic therapy. Examination at this time revealed a normal vagina and cervix. The uterus was slightly below normal in size, and a right cystic ovary, approximately 8 by 8 by 5 cm., and a slightly enlarged left ovary were palpated.

The patient measured 5 feet, 7 inches in height and weighed 142 pounds. There was no evidence of hirsutism. Hemogram and urinalysis were within normal range. The vaginal cytologic examination showed low estrogen effect with a predominance of intermediate cells. The buccal smear showed 65 per cent of cells containing the sex chromatin body. The follicle-stimulating hormone (FSH) determination showed less than 3 mouse units; 17 ketosteroids were 11.4 mg. per cent, and T-3 14.3 per cent. A culdoscopy was considered but inasmuch as the right ovary was definitely enlarged, dilation and curettage of the uterus and exploratory laparotomy were performed. A very small amount of endometrium was obtained on curettage. The cystic right ovary gave the appearance of a Stein-Leventhal ovary. The same finding was present in the left ovary. Bilateral wedge resection was performed and, on incision into the right ovary, a dermoid cyst was discovered and resected. A wedge resection of the left ovary also revealed a polycystic ovary, but no evidence of a dermoid cyst was seen.

The patient made an uneventful recovery and was discharged from the hospital on the seventh postoperative day. Exactly 28 days following surgery the patient had her first normal menstrual period without further therapy. The menses was of 5 days' duration and had occurred regularly each month. The last examination was done on May 7, 1966.

*Pathological findings.* The endometrium was scanty. The glands and stroma appeared inactive with no evidence of active proliferation or of secretory activity. The appearance of the endometrium resembled that often seen in the menopausal age group. Both ovarian wedges had thickened opaque capsules which contained excessive collagen. In the underlying stroma there were follicular cysts of varying size as well as primordial follicles. Corpora fibrosa, some cystic, were observed, but no corpora lutea or corpora albicans were present. Hyperplasia of the theca interna, sometimes prominent in these cases, was not observed, but there was striking luteinization of the theca interna cells of some follicles. The dermoid cyst of the right ovary measured about 5 cm. in diameter and contained hair and sebaceous material. A hillock composed of fibrous tissue and fat was present in the wall. The dermoid cyst was partly lined by stratified squamous epithelium with focal disruption of the epithelium; in these areas the fibrous tissue of the wall was chronically inflamed. Many macrophages and foreign body giant cells were present. Elsewhere the cyst wall contained skin appendages including hair follicles, sweat glands and sebaceous glands.

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## Discussion

Bilateral polycystic ovaries is a non-neoplastic abnormality and results from an endocrine disturbance of obscure etiology. Several theories on etilogy include overproduction of luteinizing hormone (LH) or interstitial-cell stimulating hormone (ICHS),[7, 8, 9] excess androgenic production by an ovary,[10, 11] and hyperbasophilism of the pituitary gland.[12]

The association of thecoma[13] and arrhenoblastoma[14] on the opposite gonad with the polycystic ovary has been reported, suggesting a similar endocrinologic pathogenesis for both conditions. Bevis[15] described a case with dermoid cyst of the ovary in which granulosa-cell tumor was present. He suggested certain granulosa-cell tumors to be teratomatous in origin. There were 2 unusual cases reported, 1 a benign dermoid cyst with dysgerminoma,[16] the other a thecoma[17] in the same ovary. These patients presented huge abdominal tumors and menstrual irregularities.

It has been stated that about 20 to 25 per cent of patients with dermoid cyst of the ovary are asymptomatic. They are discovered, usually on routine physical checkup or other nonrelated disorders.[4]

Our patient sought medical care because of delayed menarche at the age of 15, at which time uterine bleeding could be elicited only by the administration of cyclic hormone therapy. No spontaneous menstruation had occurred at 17½ years of age. She presented bilateral enlarged ovaries with cystic tumor of the right ovary. The pathologic diagnosis was benign adult cystic teratoma with bilateral polycystic ovaries. If one accepts the frequency of polycystic ovaries among infertile women to be 0.6 to 4.3 per cent[3] and the dermoid cysts to comprise from 5 to 25 per cent of all ovarian tumors,[5] it would be reasonable to guess that the combination in our case is fortuitous. Undoubtedly the associated dermoid cyst had no bearing on the symptoms in this case.

## Summary

A 17½-year-old woman with a chief complaint of primary amenorrhea was found to have bilateral polycystic ovaries and a benign cystic teratoma in 1 ovary. To the best of our knowledge this is the first case to be reported.

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# Vasa Praevia

## Report of a Case and Brief Review of the Clinical Features

JORGE E. MEDINA, M.D.,* AND CHARLES E. TOWNSEND, M.D., F.A.C.O.G.†

THIS EXTREMELY RARE obstetrical complication is usually followed by a high fetal loss and is probably the greatest single cause of fetal mortality for any of the "accidents during pregnancy." Less than 100 cases have been reported in the medical literature. In the greater majority this condition was unsuspected and was diagnosed after delivery. This may explain why so few cases have been reported.

We considered it worthwhile to report a case treated recently at Columbia Hospital for Women and to review very briefly the clinical features of this condition.

### Report of Case

Mrs. M. S., a 24-year-old white woman, gravida II, Para 0, was admitted to Columbia Hospital for Women on March 22, 1964 at 8:00 a.m. in early labor with a floating presenting part. At this time the cervical os was 4 cm. dilated with the membranes bulging. Pelvimetry revealed a normal pelvis. Consultation was obtained because of the station of the presenting part. It was thought that the patient would deliver vaginally. Amniotomy was performed at 9:30 a.m. At the time of the rupture of the membranes it was discovered that this patient had polyhydramnios. There was about 3,000 c.c. of amniotic fluid released. The fluid was blood-tinged at first, and frank blood was observed at the end of the procedure. Reëxamination in 10 minutes revealed a low-lying posterior placenta; there was no cord palpable. At this moment the fetal heart rate was noted to have decreased greatly and was still regular. Oxygen by mask was given, but the fetal heart tones remained poor and bleeding continued. It was decided to deliver the patient by immediate cesarean section because of the marked fetal distress and vaginal bleeding. A live, 5 lbs., 2 oz. female infant was delivered by low cervical cesarean section 47 minutes after the membranes had been ruptured.

The infant was pallid, had poor reflexes, and appeared to be in shock. Examination of the membranes and the placenta revealed a velamentous insertion of the cord and vasa praevia (figure 1). Several vessels had ruptured, thus allowing the baby to lose blood. The infant was given an immediate blood transfusion of 70 c.c. of unmatched O-negative blood through the umbilical vein. The infant responded promptly to this treatment, and her condition appeared satisfactory. She was taken to the premature nursery for further care and observation. Within the first 24 hours a diagnosis of tracheo-esophageal fistula, type III, was made on the infant. The polyhydramnios was considered to be related to this congenital anomaly and not to the velamentous insertion of the cord. The child was transferred to Children's Hospital for definitive surgery. At this time her hematocrit was 42 per cent and the white blood count 6,800. A gastrostomy was performed on that day, and end-to-end anastomosis of the esophagus was done on March 26, 1964 Following surgery she developed aspiration pneumonia which responded to the use of antibiotics. A stricture developed at the anastomosis site on May 1. The proximal end of the esophagus was exteriorized and the stomach cardia closed. The child died 50 days after birth from massive respiratory complications. The mother had an uneventful postoperative course.

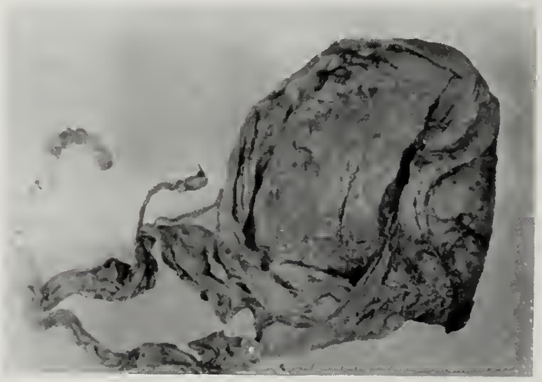

**FIG. 1. Placenta with velamentous insertion of the cord and vasa praevia. Notice rupture of umbilical vessels before they form the umbilical cord.**

### Discussion

Wrisberg in 1773 described for the first time an entity called velamentous insertion of the cord. In 1801 Lobstein first recognized the serious relationship of velamentous insertion to hemorrhage involving fetal death. Vasa praevia occurs usually in the presence of velamentous insertion of the cord. The incidence of velamentous insertion is 0.4 to 1.25 per cent according to different authors.[1, 2] It is well accepted that velamentous insertion is 9 times more common in twins[3] and almost constant in triplets or quadruplets.

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Blakiston's New Dictionary defines vasa praevia as "presentation of velamentous vessels across the internal os, seen with low implantation of the placenta."[4] Evans[5] defines it as "a condition in which the fetal blood vessels, unsupported by either umbilical or placental tissue, traverse the fetal membranes of the lower uterine segment in front of the presenting part."

Torrey[6] divides fetal bleeding into 2 groups: (a) Vasa praevia, in which, by definition, the umbilical vessels pass across the internal os and act as a barrier, albeit a fragile one, to the presenting part. The vessel may or may not be ruptured. (b) Abruption of the umbilical vessels. This includes the cases of rupture of shortened umbilical cords and those in which the cord appears normal and the condition of vasa praevia does not exist.

We found several cases reported as intrapartum rupture of the umbilical vessels without vasa praevia,[7-10] which fit within the type B of Torrey's classification because they present the same clinical picture, fetal distress and vaginal bleeding, and should be handled in the same manner.

Fetal distress may be caused by hypoxia, due to compression of the vessels against the bony pelvis by the presenting part, or fetal hemorrhage, due to rupture of the vessels before or during labor, which may cause exsanguination of the fetus.

The diagnosis is extremely difficult to establish prior to delivery. The only clinical evidence may be the sensation of the pulsating vessels within the circle of the dilated cervix.[11] From the practical point of view this is very seldom accomplished (only 4 times in the 51 cases mentioned by Emmrich[12]). A high index of suspicion is the best diagnostic weapon. The onset of painless vaginal bleeding prior to or at the time of rupture of the membranes, especially if accompanied by alterations of the fetal heart without any changes in the pulse and blood pressure of the mother, may lead one to suspect this condition. Entities which cause bleeding in the last trimester of pregnancy, such as placenta praevia, abruptio placenta and cervical lesions, must be ruled out. Bleeding is not always present because vasa praevia may occur with intact membranes,[13] or vessels may rupture before the membranes, with an intra-amniotic hemorrhage.[14] The presence of fetal distress in the absence of any obvious explanation suggests the occurrence of this condition.

A blood smear for the presence of fetal blood elements has been mentioned as a diagnostic aid.[6, 11] Israel[15] suggests the use of the Apt test,[16] which is based on the characteristic resistance of fetal hemoglobin to alkali. This is a reliable and easy test to perform. Two to 3 ml. of bloody material is mixed with equal amounts of water and centrifuged for 2 minutes at 2,000 rpm; the supernatant fluid is decantated and 1 part of 0.25 N. sodium hydroxide is added to 5 parts of the decantated solution. Within 1 to 2 minutes a yellow-brown color appears if the blood is maternal in origin; the red color remains if fetal hemoglobin is present. It must be remembered that sickle-cell anemia and thalassemia may give rise to misleading results because of the presence of hemoglobin F in the mother's red blood cells.

The prognosis for the mother is excellent, since she is not affected by the condition. For the fetus the prognosis is grave. Evans[5] reported 73 per cent of fetal loss when vessels had been ruptured before delivery. When the vessels do not rupture until the time of delivery the prognosis depends on the severity and the duration of the hypoxia to which the fetus was exposed during labor. The perinatal mortality varies between 18 and 60 per cent.[6, 12]

Inasmuch as the mother is not affected by this condition, the treatment should be directed toward saving the life of the fetus. Williamson[11] in 1912 advised cesarean section if the membranes are still intact; Evans[5] in 1952 concurred. Kosmak[17] in 1922 considered cesarean section as a too radical approach. Rucker and Tureman[1] in 1945 recommended version and extraction as the method of choice. In 36 cases reported by them only 2 cesarean sections were performed, one for prolapse of the cord and the other for the mistaken diagnosis of placenta praevia. In both cases the fetus was saved. The remaining fetuses were delivered by forceps or spontaneously.

We agree with Torrey that if the baby is still alive and a vaginal delivery is not possible within a very short period, cesarean section is a life-saving procedure. If the baby is affected by anemia, as in the present case, a prompt blood transfusion has been recommended by several authors.[1, 9, 12, 18, 19, 20] Crossmatch should be done, but if the condition of the infant is too critical O-negative, unmatched blood of low titers may be transfused as an emergency procedure.

## Summary

The presence of painless vaginal bleeding during labor accompanied by fetal distress without changes in the vital signs of the mother can be considered as a clinical syndrome which may be caused by several abnormalities of the cord, such as velamentous insertion with or without vasa praevia or spontaneous rupture of the umbilical cord (in the absence of velamentous insertion) due to cord shortness or inflammation.

Since this syndrome is followed by a very high perinatal mortality, which may be prevented if prompt diagnosis is established before delivery, a high index of suspicion of the condition is necessary. The Apt test may be used as a valuable diagnostic aid to determine the origin of the blood to substantiate the clinical diagnosis.

We feel very strongly that prompt cesarean section is indicated when vaginal delivery is not feasible within a very short period in order to secure a living infant.

The review of the literature available reveals no other case of a congenital defect associated with vasa praevia. The congenital malformation of this infant, tracheo-esophageal fistula, is the first case reported of this association and probably has little clinical significance.

The authors wish to express their appreciation to Dr. William J. Jaffurs, Director of the Department of Pathology at Columbia Hospital for Women, for supplying the photograph and for the valuable suggestions in the preparation of this manuscript, and to Mrs. Ursula E. Selinger for typing the manuscript.

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### Familial Neutropenia—Feroli

(*Continued from page 745*)

From the foregoing it is obvious that the basic defect in neutropenia of any variety is unknown. The presence of large atypical myelocytes in the bone marrow of the index patient suggests an anomaly in granulocyte maturation although a plasma factor must also be considered.

## Summary

A 10-month-old microcephalic white female was found to have persistent neutropenia with a normal total white blood cell count and a normal bone marrow study. Studies of granulocyte kinetics were normal. She had no serious infection.

A similar peripheral blood finding was present in the patient's 2 siblings, her mother, maternal uncle, and maternal grandfather. A bone marrow smear taken from the mother was normal. None of the family had serious or frequent infections.

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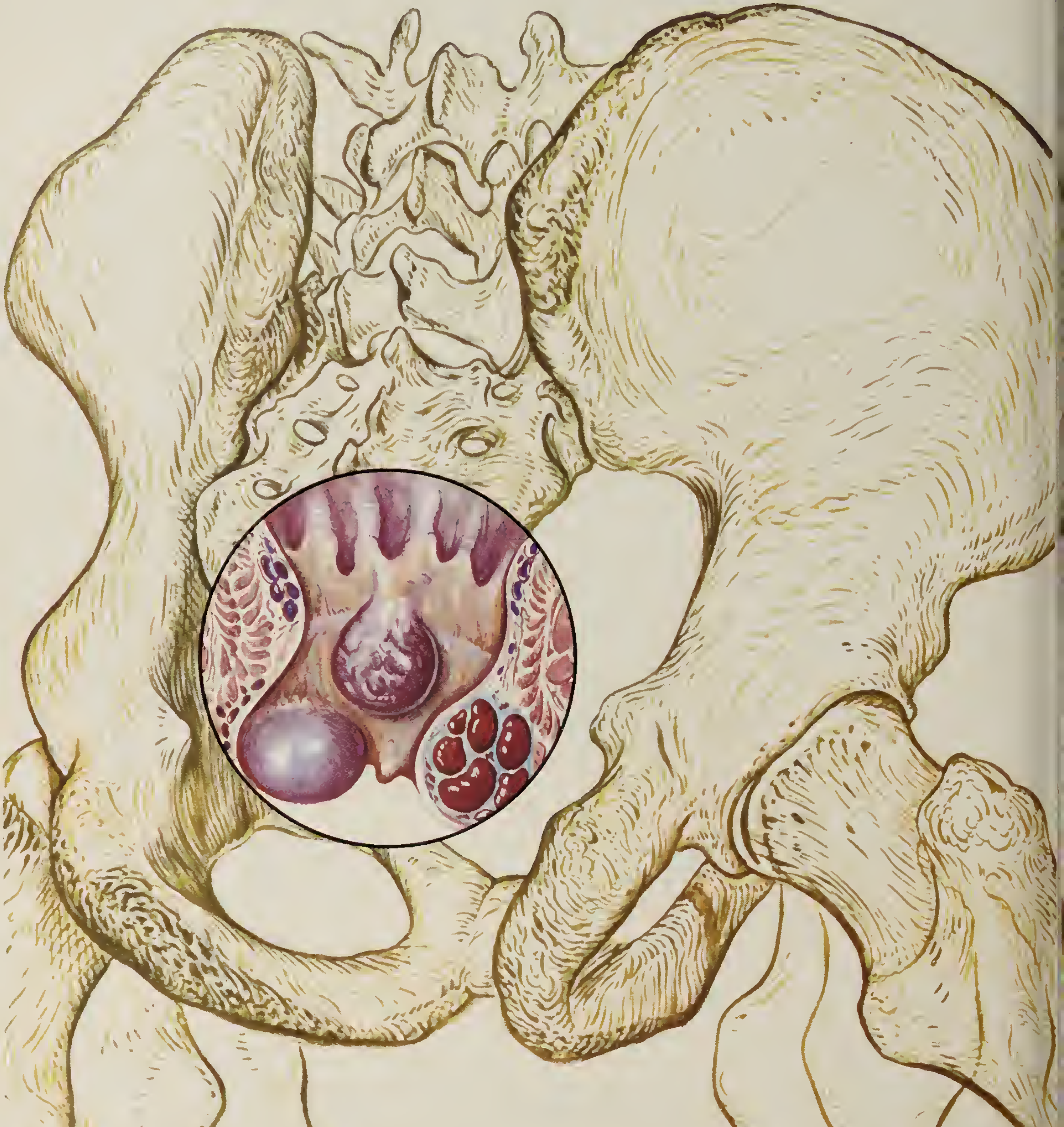

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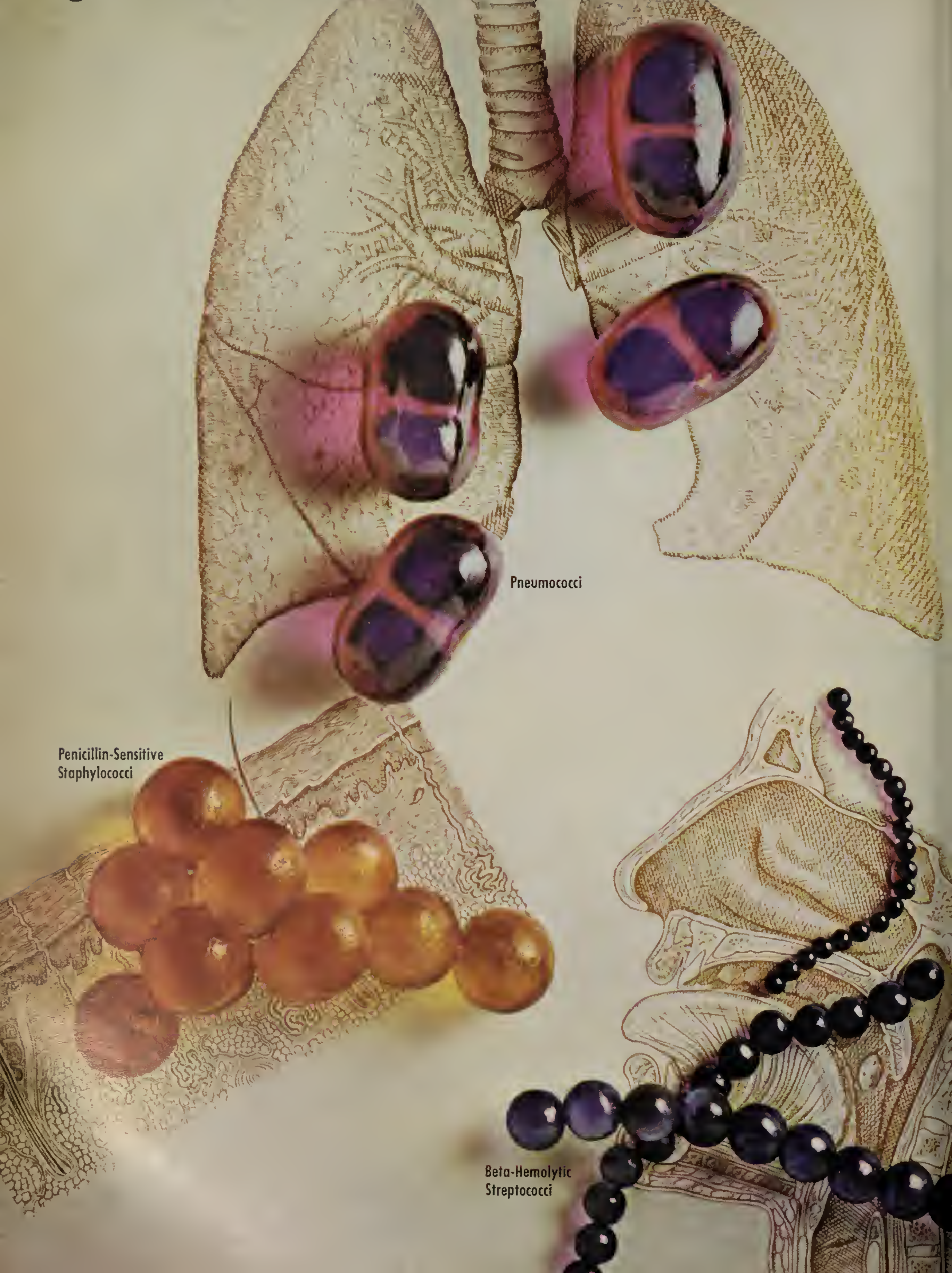
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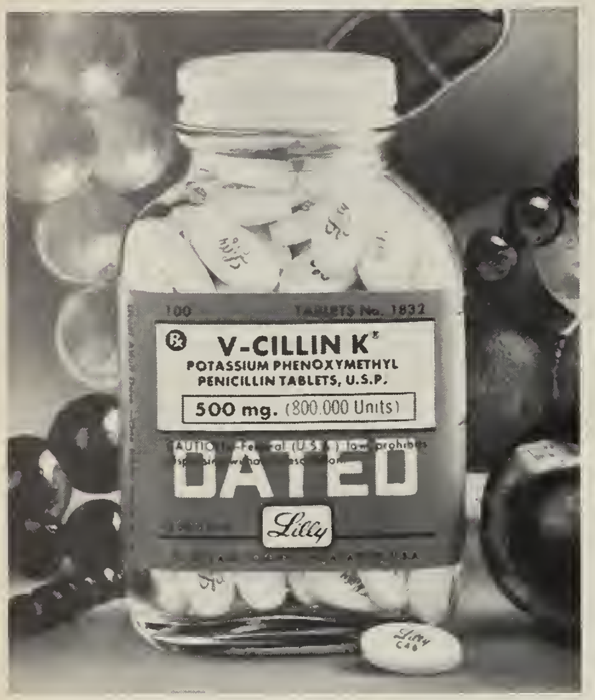

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**Contraindication:** Penicillin hypersensitivity.

**Warnings:** In rare instances, penicillin may cause acute anaphylaxis which may prove fatal unless promptly controlled. This type of reaction appears more frequently in patients with a history of sensitivity reactions to penicillin or with bronchial asthma or other allergies. Resuscitative drugs should be readily available. These include epinephrine and pressor drugs (as well as oxygen for inhalation) for immediate allergic manifestations and antihistamines and corticosteroids for delayed effects.

**Precautions:** Use cautiously, if at all, in a patient with a strongly positive history of allergy.

In prolonged therapy with penicillin, and particularly with high parenteral dosage schedules, frequent evaluation of the renal and hematopoietic systems is recommended.

In suspected staphylococcus infections, proper laboratory studies (including sensitivity tests) should be performed.

The use of penicillin may be associated with the overgrowth of penicillin-insensitive organisms. In such cases, discontinue administration and take appropriate measures.

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# PRESIDENT'S PAGE

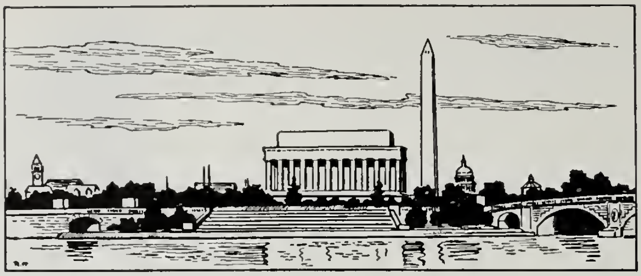
## THE YEAR IN REVIEW

During the year of indoctrination and education as President-elect, your President surveyed the interests and functions of the Society in order to develop a plan for his administration and to construct an approach to specific areas for progress in our affairs as they relate to the needs of the profession as well as to the community at large. Attendance at meetings of the 40-odd committees helped create some understanding of the wide variety of problems in which the Medical Society is involved. Some of these activities are ongoing, requiring continuing supervision and guidance. Some are current, to be disposed of in a relatively short time. Some are new, demanding thought and imagination, research, and consultations in other fields to develop organizational planning for initiation of appropriate action. The following résumé constitutes a report of our activities during our 150th Anniversary Year.

This was the first year of action with respect to the Regional Medical Program. The MSDC is the Grantee for the Metropolitan Washington Area under P. L. 89-239 and as such has the responsibility for development of area participation in the Heart, Cancer and Stroke Programs as projected in that legislation. A highly competent coördinator, Dr. Thomas W. Mattingly, was chosen. He has confirmed our confidence in his ability by carrying forward initial research studies in needs, resources, personnel and facilities to lay the foundation for future operational activities. Planning phases as well as essential basic administrative structure have taken shape, so that with active participation by all the included area medical schools, hospitals and county medical societies, it is hoped that these efforts will in the year to come be translated into projects which will yield benefits to the profession and the public. It is hoped also that our attempt to combine in united effort the unique diversity of jurisdiction, geography, allegiance and interests peculiar to this area will be rewarded by the achievement of significant practical benefits for all concerned.

Our Medicolegal Committee has established closer liaison with the D. C. Bar Association, with the expectation of greater mutual benefit in the future. Modification of a change in local law governing licensure in the District of Columbia in order to facilitate staffing of the D. C. Department of Health as well as local medical schools and hospitals has been discussed and presented to the District Committees in the House and Senate. Bills concerned with the practice of optometry have received attention and recommendations from appropriate Sections of the Society. Statements urging action directed toward elimination of air pollution have been published and sent to Congress. Discussions leading to recommendations regarding water pollution and refuse disposal have also been held, at a more basic level, indicating the concern of the Society in these vital community health problems. In this same general area might be mentioned participation by the Society in developing standards for driver fitness, survey of administration of school health needs, endorsement of implementation of Title XIX (Medicaid) to include free choice of physician and hospital (or clinic), and the beginnings of a vigorous effort to overhaul the entire structure and law pertaining to the District Board of Licensure. Time and space prohibit detailed exposition of these matters, but be assured that your Society is taking an active part.

(*Continued on page 762*)



# EDITORIALS

*December with her icy hand tears down fall's gold and russet curtain, and on a stage bereft of props dares us to be gay. Christmas is the answer to that challenge.*

## Head Start Medical Consultation Program

In a new partnership between the Office of Economic Opportunity and the American Academy of Pediatrics, the Academy will organize and direct the Medical Consultation Program of Head Start child development programs in nearly 2,000 communities throughout the United States.

Dr. Robert S. Mendelsohn, a pediatrician from Chicago, and formerly director of Project Head Start of the Cook County Office of Economic Opportunity, will direct the program.

Sargent Shriver, Director of OEO, welcomes the wholehearted support offered to the program by the Academy, which represents more than 10,000 pediatricians in the United States, Canada, and Latin America. The AAP, to a large extent, has set the standards for child health care both in this country and abroad.

This contract represents a new type of relationship between an agency of the Federal Government and a voluntary professional organization. In effect, the American Academy of Pediatrics has accepted a major responsibility for ensuring that the health services provided to Head Start children adequately meet the health needs of these children, their families, and the communities in which they live.

Initially, the AAP will select about 300 physician-consultants from its membership and from other leaders in the field of child health to evaluate the medical aspects of the Head Start program at the state and local level. As more physicians gain experience in working in community health programs, their increased skills and knowledge will make their advice more valuable in planning and carrying out those programs which require a partnership between physicians and Government.

Each medical consultant selected will work with the medical director and other health professionals. He will review the medical aspects of Head Start applications submitted by a community; meet with local planning committees to map out Head Start medical programs; maintain contact with program medical directors; follow up and evaluate programs, and maintain liaison with OEO regional and national offices.

Consultants will work with the Office of Economic Opportunity representatives responsible for funding and evaluating Head Start health programs, helping them interpret the needs of the children, the resources of the community, and the success of the Head Start programs. The consultant will supplement, rather than replace, the medical and administrative skills available in each community.

The Academy's Executive Board and staff are enthusiastic about the opportunity this program offers for developing responsible pediatric leadership in an important area of child health programming. This is an activity which will most certainly expand and could set an important trend in the programs of medical organizations.

AAP's broad experience and capacity for developing comprehensive child health programs will enable the Academy to provide medical supervision which will ensure excellence and quality in the health services provided under Head Start programs.

William S. Anderson, M.D.
*President, American Academy of Pediatrics*

# FDA Prescription for Prescription-drug Advertisements

or

How's That Again?

The Pharmaceutical Manufacturers Association and the Food and Drug Administration have reached an out-of-court agreement on the question of whether the generic name must be used every time the brand name appears in advertising or promotion. The issue had reached the Supreme Court, which ruled that it should be reconsidered in the lower courts. On the basis of the settlement there probably will be no further court action. Under the settlement by PMA and FDA, the amended regulations published in the Federal Register for October 27 propose:

"If an advertisement for a prescription drug bears a proprietary name or designation for the drug or any ingredient thereof, the established name, if such there be, corresponding to such proprietary name or designation shall accompany such proprietary name or designation each time it is featured in the advertisement for the drug; but, except as provided below in this subparagraph, the established name need not be used with proprietary name or designation in the running text of the advertisement. On any page of an advertisement in which the proprietary name or designation is not featured but is used in the running text, the established name shall be used at least once in the running text in association with such proprietary name or designation and in the same type size used in the running text:

"*Provided, however,* That if the proprietary name or designation is used in the running text in larger size type, the established name shall be used at least once in association with, and in type at least half as large as the type used for, the most prominent presentation of the proprietary name or designation in such running text. If any advertisement includes a column with running text containing detailed information as to composition, prescribing, side effects, or contraindications and the proprietary name or designation is used in such column but is not featured above or below the column, the established name shall be used at least once in such column of running text in association with such proprietary name or designation and in the same type size used in such column of running text:

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PMA President C. Joseph Stetler said he was "happy that an agreement had been reached that satisfactorily resolved the differences between the industry and the FDA."

# A Society for Medical Historians

The Washington Society for the History of Medicine was formed in February 1961 by a group of individuals in the Greater Washington Area who share an interest in the history of medicine and allied sciences. The Society, an affiliate of the American Association for the History of Medicine, meets bimonthly, except during the months of June, July and August, and attempts to present an interesting and varied program of historical papers. The speakers include members of the local society as well as outstanding historians who are invited as guest speakers at least twice a year. Previous guest speakers have included Owsei Temkin, Rene Dubós, Lloyd Stevenson, and Lester King. Individuals in the Greater Washington Area who are interested in presenting papers are urged to submit them.

The bimonthly meetings, which begin in September, are held in the Billings Auditorium of the National Library of Medicine. Interested persons are requested to contact the Secretary-Treasurer, Dr. Peter D. Olch, whose address is the History of Medicine Division, National Library of Medicine, 8600 Rockville Pike, Bethesda, Md. 20014 (phone 496-5961). Annual dues for the Society are $3.00.

Jeanne L. Brand, Ph.D.
*President, The Washington Society for the History of Medicine*

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# Question of the Month—?

**The American Medical Association has recently issued a policy approving doctors' listing their specialties (limited to those specialties approved by AMA) in the Yellow Pages of the telephone directory. Do you think this is a good idea?**

### Answers and Comments

MITCHELL W. SPELLMAN, M.D. (Thoracic Surgery): I endorse the policy which approves the listing of the specialties of physicians in the Yellow Pages of the telephone directory.

The proposition that physicians' professional interests are not fundamentally different so that specialty classifications among the telephone listings are unnecessary is in contrast to the preponderance of specialists. The failure to identify the specialties of physicians obscures an authentic reflection of the composition of the local medical community.

Some claim that physicians protect the public interest by withholding designations of specialties from the telephone directory. They speculate that an ingenuous patient is a candidate for exploitation by an unscrupulous physician who misrepresents his area of competence. The Yellow Pages of the telephone directory would ostensibly aid the unprincipled physician to beguile a credulous public and thus to debase his profession.

This largely disregards the controlling influence of hospital staff memberships whereby the practice of specialists is circumscribed. Outside the hospital, the compliance exacted by professional societies and the legal sanctions upon malpractice assure restiraint by physicians. These considerations should discourage the tendency to exaggerate the vulnerablity and naïvete of the patient in an informed society and to project medical organizations into the self-conscious role of guardians of morality.

Resistance to an innocuous change in the public policy of the Medical Society, such as is entailed here, should not be supported upon a premise of retaining ethical values that have little current pertinence.

JOHN M. KESHISHIAN, M.D. (Thoracic Surgery): Yes.

Very often patients have been given the name of a specialist to consult in a distant city if the need ever arises. On that occasion the patient may not be able to remember the physician's name nor locate the referral slip. However, a quick check through the Yellow Pages with a specialist so listed may jog the memory.

In addition, listing by specialties can save needless phone calls from new arrivals in Washington who are seeking a personal physician. With the large turnover of the populace here in Washington, this no doubt frequently occurs if we are guided by the number of patients seeking a specialist who call the MEDICAL BUREAU.

Additionally, there are many physicians listed in the Yellow Pages who are not in the active practice of medicine. If physicians are listed by specialties or a particular specialty of medicine in which they choose to work, it would streamline this list so that it would become of greater benefit to the patient.

CHARLES P. RYLAND, M.D. (General Practice): I do not agree wholeheartedly with the AMA policy. While Chairman of the Medical Bureau Committee we discussed this several times. It certainly has its advantages in that the public can open the telephone book and pick out the specialty he desires, provided he has made the right diagnosis. The disadvantage of the specialty listing is the possibility of the physician requesting listing in a field in which he is not fully qualified. This may be minimized if the telephone company will only include those specialty listings approved by the local Medical Society. Our telephone company here agreed to do this for us if we approve the specialty listing.

SAMUEL DOVE, M.D. (General Practice): It seems logical that the public should be allowed to know the type of practice as well as the telephone number of doctors listed in the telephone directory. This identification would allow the prospective patient to see the names of all physicians in the area and in the specialty he seeks. A side benefit should be a considerable lessening of the MEDICAL BUREAU switchboard workload.

Perhaps some doctors who do not specialize might be concerned about a loss of prestige under the new system. As for the occasional improper self-designation of an unqualified physician, our present self-policing activities, reinforced by hospital standards in selecting staff members, should continue to operate as a safeguard to the public and the profession.

I believe that we who do general practice have, by our scarcity of numbers alone, a much wanted "specialty." Furthermore, the emphasis will not be on what the doctor does but on how well he does it.

CHARLES E. TOWNSEND, M.D. (Obstetrics-Gynecology): No. Listing specialty in the Yellow Pages would be a duplication of a service already provided the public by our Society. Directory listing might be of value to the few physicians who are not Society members, but for them who would assign a category?

GEORGE S. VOUVALIS, M.D. (Ophthalmology): Yes, for each specialty in alphabetic order.

**If any members have dissenting views, your Editorial Staff will be pleased to receive and publish them.**

### President's Page: The Year in Review

*(Continued from page 757)*

We feel that a crying need of the community is about to be met by the creation of an Interdisciplinary Committee on Drug Dependency under the aegis of the Society which will include representation from medicine, dentistry, pharmacy, the judiciary, enforcement agencies, the legal profession, and other social and governmental groups concerned with this problem. Formative stages are complete; mutual discussion and liaison can now, we believe, develop more satisfactory coördination in attacking a currently splintered, ineffective approach to a growing menace to community health.

During the year the Society has also engaged in more temporary activity, while hoping for permanent effect, in actions to promote resolution of problems involving the American Red Cross Blood Program and the Metropolitan Washington Blood Banks, Inc., to strengthen liaison with the Woman's Auxiliary to the Medical Society of D. C., and to achieve more effective interchange of patient care between the D. C. General Hospital and the community hospitals.

Staff activity has been carried forward with energetic imagination by our uncommonly able Executive Director, George W. Cooley, to produce a more efficient, streamlined administration. All in all, it has been an interesting and stimulating year. I sincerely hope that my efforts have been of value to the Society. I am sure much more might have been accomplished by one of greater experience and capacity. Problems presenting a real challenge and not yet dealt with include shaping a more satisfactory coöperation between physicians and Blue Shield and a realistic attack on the broad question of the management of alcoholics, which, I believe, should be given top priority by my successor. To the past, "*Vade*"; to the future, "*Ave.*"

Henry D. Ecker

# One Hundred and Fiftieth Anniversary of The Medical Society of the District of Columbia: A Brief History

MICHAEL J. HALBERSTAM, M.D.*

MEDICAL HISTORY has clinical as well as social importance, for it reminds us of both the eternal nature of some of the problems we face and the transitory importance of some of the remedies we hold dearest.

The members of the Medical Society of the District of Columbia who celebrated its 75th Anniversary in 1894 with a dinner of oysters, puree St. Germaine, shad roe, spring lamb, terrapin, salad, cheese, ice cream, cake, and wines may not have had the use of Benemid® and Compazine®, but they well knew the pains of eating and drinking too vigorously. Their patients had, and our patients have, much the same problems, although it must be noted that since 1894 typhoid has disappeared from the District of Columbia and myocardial infarction has made itself known. Some new diseases and many new remedies will have disappeared and others will have been discovered by the time this Society celebrates its 200th Anniversary in 2017, but it is unlikely that the basic engineering of the human body—and the infinite number of ways in which this engineering can go wrong—will have changed much. Even less likely is the possibility that the ways in which humans deliberately torment their own bodies and minds with drugs, alcohol, envy and greed will be much altered. The founders of our Medical Society back in 1817 could step into our offices today and make a fair enough diagnosis in many of our cases, and if it is any consolation, perhaps we would be able to do as well in 2017.

The men who founded the Medical Society of the District of Columbia were acting primarily to form a guild and to protect the public and improve their own social, scientific, and economic interests. They were concerned about the prevalence of "charlatans," who, in the words of one of the Society's early historians, "not only imposed on the citizens, but worked a hardship, as such pretenders always do, to the regularly qualified physicians." Nevertheless, when the Society was chartered by Congress in 1819 it was for "promoting and disseminating medical and surgical knowledge and for no other purpose whatever." The Society was given the right to control licensure of physicians but was forbidden to regulate fees or in any way to regulate medical practice or ethics. The Society met regularly at various inns and taverns during its first few years, and papers were presented and cases discussed, but gradually interest waned. In 1833 a separate organization called the Medical Association of the District of Columbia was established without Congressional charter. It had essentially identical membership with the Medical Society, but it could and did set fees that could be called "usual and reasonable" in today's parlance. A visit and prescription was $1.00, consultations $5.00, and obstetrical cases $12–15.00. This Society continued to promulgate a fee schedule until 1934.

Until 1911 the Medical Association and the Medical Society continued to ply their separate but parallel ways, the former concerning itself with the ethics and economics of practice, and the latter with the scientific aspects of medicine. Thus, in one of its earliest resolutions, which would come back to divide the Society 100 years later, the Association in 1833 declared itself against contract practice. This was a method by which physicians attended a family or individual on a yearly prepaid basis, which even in 1833 was used by some prominent physicians and families. The Association also strictly forbade its members to consult or associate professionally with non-member physicians. This rule helped force all reputable physicians in the District to belong to the Association and was an effective way of keeping dissident members in line. When in 1871 a maverick member called in a non-member to consult in an important case (the patient was the Vice President of the United States), he was expelled from the Association, his practice melted, and he had to humbly beg forgiveness before reinstatement.

The Association also concerned itself with the tendency of military physicians stationed in Washington to establish private practices after hours in addition to their official duties. These so-called "sundowners" flourished particularly in the peaceful, sleepy post-Civil War military community.

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* Clinical Instructor in Medicine, George Washington University School of Medicine; office: 2520 L Street, N.W., Washington, D.C. 20037.

The ambivalent relationship between private and government physicians continued until a few years ago, and now government-employed physicians may be full Active members with all privileges. It is Washington's special version of the town-gown division where there are 2 large groups of professional men, alike in training and intelligence but dissimilar in types of employment, means of advancement, and possibly temperament. The Society has always respected and often honored the distinguished physicians who have worked for the Federal Government and other organizations in the Washington area, but on the other hand it has always been aware, as an earlier writer noted, that there were more salaried than privately practicing physicians in the District of Columbia, a situation which exists in no other large city.

In early years neither the Society nor the Association was open to all qualified physicians in private practice in the city. The admission of female members aroused great debate during the 1870's and 80's when the first 2 women graduates began their practices in the city. Both medical groups refused membership to these women on various grounds, pointing out that the Society's Congressional Charter spoke of the limitation of practice to "gentlemen." It took an Act of Congress, but in 1885, 10 years after they had been given full licensure in the District, Drs. Mary A. Parsons and Mary D. Spackman were admitted to the Society.

It may or may not surprise the current membership to know that as far back as 1869 the admission of Negro members to the Society was proposed, and that during the 1870's a sizable percentage of the membership supported this idea. An attempt was made by Senator Sumner of Massachusetts to have the Society's Congressional Charter revoked because of discriminatory practices, but neither this effort nor the attempt to gain Negroes membership succeeded. The Society did unbend enough, however, to permit for the first time consultation with qualified Negro physicians. This was during the post-Civil War period when, as Washington historian Constance Green has pointed out, freed slaves and educated Negroes were making an attempt to take an equal and unseparate part in the City's life. Official segregation ordnances did not come into existence for another 15 or 20 years. It would be interesting to speculate on how the City and the Society would have developed if Negro physicians had been accepted earlier. However, Southern sentiment predominated in the City, and some of Washington's eminent post-war physicians had served on the Confederate side. One, Alexander Yelverton Peyton Garnett, had been personal physician to Jefferson Davis and most of the Confederate Cabinet. With this in mind, we might respect more fully the fact that in another attempt to break the color bar a Negro physician with influential backing from within the Association received a majority of 76 votes out of 124 for membership in 1894, but two-thirds support was required.

In the close-knit medical world of the 19th Century there were no specialists, no specialty societies, no national or international meetings to be attended by jet on a long weekend, few journals, and fewer visiting lecturers at the medical schools. The postgraduate education of physicians, which today takes place in a dozen different ways, was centered primarily in the local medical society. The Medical Society of the District of Columbia met and debated the treatment of puerperal fever by opium. The Society encouraged the practice of vaccination—in the 1840's still a controversial subject. Interesting cases were presented at Society meetings, culminating in 1856 when William Beaumont turned up with Alexis St. Martin in tow. The meeting was well attended, as one would assume it would be if it were held tomorrow.

The Society was active in matters of public health. It pressed for a registry of birth and deaths, fought the cholera epidemic in the summer of 1832 (459 deaths), supervised the purity of milk and water supplies, and since 1886 regularly proposed that the District find some more effective way of treating alcoholism.

The early records of the Society remind us of an era when meals were enormous, speeches flowery and full of naïve self-congratulation, and expectations Utopian. The general belief was that if all the City's streets could be lighted electrically the millenium would have arrived. The medical and social dangers of affluence were not yet foreseen. Speakers at the Society's dinners in 1894 and even in 1917 went on almost endlessly about the great accomplishments of the Society, of the medical profession, and of the United States. To reread those speeches—complete with jokes about mythic Irishmen, Jews and Negroes—is to be reminded of the careless optimism of the times when "more" automatically meant "better." Now that we have more we're not so sure. But good qualities emerge from those earlier years—the esprit de corps in a medical society in which all the members knew one another personally and were aware that misconduct of one would affect all, where the mystique of medicine and its priestly aspects were taken more seriously, and where love of one's profession and country were as unself-consciously paraded as we today describe our family's exploits.

After World War I the Society moved rapidly toward the problems and challenges that still face us. The Society and Association were combined in 1911, and in 1920, under the leadership of Dr. Edward Y. Davidson, construction was begun on the building at 1718 M Street, which was to become the first permanent home of the Society. Physicians from the City had served bravely both with American and British forces in the Great War, but it is interesting to note that although only 1 physician was killed while on active duty, 5 Active members of the Society died within 2 weeks' time during the influenza epidemic of October 1918.

A Woman's Auxiliary to the Society was formed in 1925 and has been vital in both the social and civic efforts of the Society ever since. During the 1920's and 1930's the Society received funds for establishing the Kober and Davidson scientific lectures, and in 1929, largely due to the efforts of Dr. Charles Stanley White, the Annual Scientific Assembly of the Society was begun. These meetings have since become so large and popular that they are held in a downtown hotel instead of in the Society's building as originally intended.

Since 1869 the Society has made an attempt to publish its proceedings and the scientific contributions of its members. This publishing by physicians is a difficult matter. After all, publishers do not practice medicine, and yet physicians, if they are to keep a record of their contributions, must do the journalistic work themselves. In the years between 1869 and 1920 a total of 8 different periodicals attempted to record the Society's business. The final effort in this line, the *Washington Medical Annals*, edited by Dr. Daniel S. Lamb, was the most successful, lasting from 1901 until undone by the First World War.

The current Medical Annals of the District of Columbia was begun in 1932 under the direction of Dr. Coursen B. Conklin and Dr. Wallace M. Yater. Beginning in 1938 Mr. Theodore Wiprud added considerable impetus to the journal. Its currently flourishing state in which there is a steady supply of articles and almost enough advertising (there is never enough of that) can be attributed in large part to Dr. Yater's continued devotion to the journal. Few publications are fortunate enough to obtain such editorial acumen at their onset and then retain it for over 35 years. Miss Louise Eckburg has helped maintain the journal's editorial clarity, and her spirited goading of its contributors has aided in getting their articles finished on time.

The late 1930's saw the District Medical Society as the defendant in a law suit which was a test case for the Nation and a bitter fight locally. In 1937 a Federal agency, the Home Owners Loan Corporation, formed with the aid of a lay board the Group Health Association in order to furnish prepaid medical care to its members. Although certainly the primary aim of the Association was to give reliable, inexpensive care to its members, some of its New Deal planners also saw it as a prototype for all of American medicine. The Medical Society had been on record against contract care since 1833. During the early 1930's it had refined and redrawn its definition of contract care, allowing doctors to participate as company or agency physicians so long as the plan was under physician control and the contracting agency did not profit from the physicians' labors. The Group Health Association did not appear to meet these criteria, and the Society worked actively against it and the physicians who coöperated with it. The American Medical Association joined in condemning the Association. The Federal Government watched attentively, and in December 1938 the Justice Department brought suit against the Society, several of its leading officers, the AMA, and several associated groups for conspiring to prevent Group Health from getting hospital facilities for its members. The suit was fought, lost, appealed, lost again, and reappealed to the Supreme Court, which upheld the previous decision. All individuals were acquitted, but the District Medical Society was fined $1,500 and the AMA, $2,500.

Almost coincident with the initial rumblings of the antitrust suit, and in part spurred on by that prospect, the Society in late 1937 authorized employment of its first full-time secretary. He was Theodore Wiprud, who assumed the job in early 1938 and who previously had held a similar post with the Medical Society of Milwaukee County and had had experience in medical society organization. His hiring was evidence that many members of the Society were concerned not only with improving its public image but also in making realistic plans to finance medical care more equitably. Mr. Wiprud served valuably until his retirement in 1962, when he was succeeded by the equally efficient George Cooley.

The Society had always been somewhat more liberal than its counterparts in the AMA's House of Delegates. In 1934 the Society endorsed and approved the local Group Hospitalization, a prepaid plan which flourishes today. In 1934, however, the idea was still new, and the AMA was less than enthusiastic. The Society showed further evidence of innovation in 1938 when it sponsored a prepaid plan for lower income workers covering some hospital and nursing service and medical and dental care. Called the Mutual Health Service, the plan operated only from February, 1939 to March, 1940. It failed for lack of subscribers, and one of the main reasons for this was that only families under a certain income level were eligible. Employers and supervisors, who themselves were not eligible, failed to spread much enthusiasm for the plan among their employees. In 1948 Medical Service of the District of Columbia was created. Among the many physicians who were influential in supporting and implementing this plan were Drs. Harry F. Dowling, Frank D. Costenbader, Donald Stubbs, and Arthur C. Christie.

During World War II the Society coöperated fully with the National Selective Service Program and with local civil defense authorities. It was during the War that the Medical Bureau, established in 1940, came into its own as an efficient method of linking patients with physicians. Many members of the Society offered their services and served in all parts of the world, returning as officers of the highest rank in recognition of the fulfillment of their medical duties and responsibilities.

Since the War has come the Society's belated but nevertheless encouraging decision to admit Negro physicians to membership. Physicians back from World War II were little inclined to accept the restrictions and traditions of the past. Although many members still opposed the move, it is significant that much of this opposition was silent—prejudice had become publicly and socially unacceptable. The pressure of the Federal Government in opening appointments in Gallinger Hospital to Negro physicians was a first step in desegregation. The statesmanship of Drs. W. Montague Cobb, Herbert P. Ramsey, Walter Freeman, and Raymond T. Holden helped make the period of debate and voting a less contentious time than it otherwise might have been. The Medico-Chirurgical Society of the District of Columbia, the Nation's first Negro medical society, still exists and continues to render valuable professional and community service, a fact which should not surprise anyone who is aware of the existence of the Jacobi Society, St. Luke's Guild and similar organizations of physicians who also belong to the Medical Society of the District of Columbia.

Physicians continue to make valuable contributions to the City's life. Dr. Preston A. McLendon served on the School Board for many years. Dr. Luther H. Reichelderfer was President of the D. C. Commissioners from 1930 to 1933. The Society and its many committees provide necessary advice to Congress, the Government agencies, and to City departments on matters ranging from air pollution to the financing and furnishing of care to the medically indigent.

In 1966 the Society moved into its new quarters on Eye Street, N.W. Indicative of the changes which have taken place in medical practice in the past 150 years is the list of other organizations sharing space in this building—the Washington Heart Association, D.C. Cancer Society, Medico-Care, and the Regional Medical Program of Metropolitan Washington. These names testify to the complexity of medical practice today, the involvement of great voluntary agencies and Federal bureaus in medical care, and the contribution that can still be made by one or two visionary men. The efforts of Dr. William B. Walsh, founder of Project HOPE, and of Dr. Peter D. Comanduras, co-founder with the late Dr. Tom Dooley of MEDICO, have made Washington a home base for physician projects abroad.

The Society now faces, like its members, the problems of urban existence, for if there are only vast tracts of office buildings and Federal beehives downtown, where will the patients live? As one of the few permanent influential groups committed to working in Washington, regardless of who is in the White House, the Society will increasingly be faced with the need to improve the quality of life in the Nation's Capital. The inquiring, scientific spirit and civic responsibility which marked the Society's past will have even more pertinence in its future.

# Health Dept. Notes

## The Chronic Alcoholic

THE CHRONIC ALCOHOLIC, as defined by the U. S. Court of Appeals for the District of Columbia, is any person who chronically and habitually uses alcoholic beverages to the extent that he has lost the power of self-control with respect to the use of such beverages or, while under the influence of alcohol, endangers the public morals, health, safety or welfare.

The March 1966 legal decision containing that definition gave added significance to the belief long held by innumerable professionals in both the health and welfare fields that the chronic alcoholic is not a criminal but rather the victim of disease.

A rule of thumb in the treatment of chronic alcoholics is that no case is curable unless the alcoholic himself will admit to excessive drinking. However, whether or not he admits it, the chronic alcoholic who comes before the courts in the District of Columbia now finds himself, in most cases, so certified. As a result of the 1966 court decision he then becomes the responsibility of the D. C. Department of Public Health.

The Department had been operating an alcoholism program since 1945 which treated as many as 700 patients in one year, most of them men. Individual and group psychotherapy were among the clinic services provided. In addition, a program of research into the causes and nature of chronic alcoholism had been established, providing specialized training for professional personnel.

Immediately following the court action, the Department began to implement plans to fulfill the court's mandate, and in November 1966 it opened the Rehabilitation Center for Alcoholics at Occoquan, Virginia. This 425-bed facility has a staff of 121 people and is used for diagnosis, treatment and rehabilitation. The program is divided into 3 phases: detoxification, therapy and work training.

Upon admission a patient is placed in the Detoxification Unit where he has a psychiatric consultation. Following laboratory tests and a chest X-ray, the need for medical care, either on an inpatient or outpatient basis, is determined.

For those who require outpatient care only, the court is requested to grant a release from the Center and the patient is assigned to outpatient treatment at the Rehabilitation Clinic for Alcoholics at 14th and Q Streets, N.W., or at the Area C Community Health Center, located on the grounds of D. C. General Hospital.

Those who remain at the Occoquan facility as inpatients are assigned to a planned rehabilitation program after 10 days in the Detoxification Unit. The patient then begins a schedule which includes group, recreational, vocational, physical, and occupational therapy and manual arts. He takes part in retraining programs, has individual counseling, and assumes certain assigned duties at the Center.

On his sixtieth day of treatment the patient joins others in a prerelease work training program, and any necessary therapy is continued simultaneously. Taken by bus to the site of outside employment, the patient is paid the prevailing rate for work performed. If he wishes Center personnel will save his earnings for him so that he may build funds with which to start anew at the end of his 90-day commitment.

Another step in the growing program for chronic alcoholics was taken in July by the Health Department when ground was broken for a Detoxification Center at 619 N Street, N.W. Expected to open at the end of this year, the 50-bed Center will provide around-the-clock care for both voluntary and arrested patients. It also will present opportunities to determine the most effective treatment for the District's chronic alcoholics.

The goals of the Health Department in its alcoholism program are assistance to the patient (1) in his understanding the reasons for his excessive drinking, (2) in handling his problems constructively, and (3) in developing the ability to remain sober when he again assumes the responsibilities of daily living.

MURRAY GRANT, M.D., D.P.H.
*D. C. Director of Public Health*

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# DOCPAC Briefs

or

## Politics and Medicine

THE QUESTION is often asked, "Should the physician involve himself in politics?" It is no longer fashionable to get involved in anything except, perhaps, riots, marches, flag burnings, and pot parties. It is therefore more important than ever that the physician set an example to other good citizens by accepting his obligation to contribute to the political activity of his community. He must take an active and effective role in public affairs medically as well as nonmedically.

But of course there are those who say, "I'm too busy. Let Joe do it," and you can be sure some Joe will do it but, unfortunately, all too often not the way it should be done.

So, better say, "Let's get busy and organize medicine into an effective political action group."

Don't delay; accept your responsibility; join the District of Columbia Political Action Committee and its parent organization, AMPAC, today.

If you are not interested in the political plight of medicine, who will be?

ROBERT S. POOLE, M.D.

## New Members

### Active

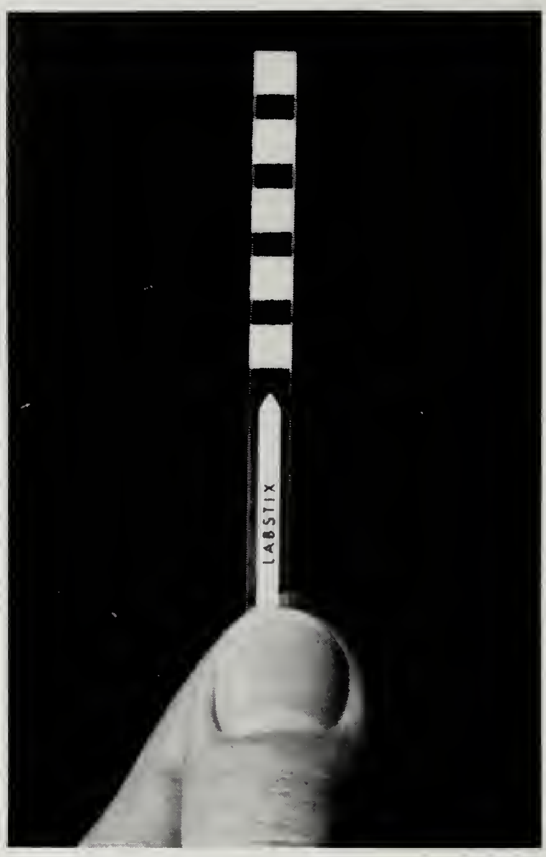
MONZER ATTAR, M.D. Office: 2121 Pennsylvania Avenue, N.W. Born in Beirut, Lebanon, he received his medical degree from the American University of Beirut in 1961. Specialty: Gastroenterology.

MARY COLEMAN BAZELON, M.D. Office: Children's Hospital of the District of Columbia. Born in Washington, D. C., she received her medical degree from George Washington University in 1960. Specialty: Pediatric Neurology.

ROBERT FRANKLIN BLYTHE, M.D. Office: 3326 Georgia Avenue, N.W. Born in Richmond, Ky., he received his medical degree from Ohio State University in 1956. Specialty: Urology.

MAURICE JEROME CASEY, M.D. Office: Sibley Memorial Hospital. Born in New York City, he received his medical degree from Georgetown University in 1959. Specialty: Surgery.

RAYMOND ELMER CONTEE, JR., M.D. Office: 1325 Upshur Street, N.W. Born in Washington, D. C., he received his medical degree from Howard University in 1959. Specialty: Internal Medicine.



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MERVYN L. ELGART, M.D. Office: George Washington University Hospital. Born in Brooklyn, N. Y., he received his medical degree from Cornell University Medical College in 1957. Specialty: Dermatology.

RONALD SHERWIN FISHMAN, M.D. Office: 1746 K Street, N.W. Born in Chicago, Ill., he received his medical degree from the University of Illinois in 1959. Specialty: Ophthalmology.

DAVID STERN FRIENDLY, M.D. Office: Children's Hospital of the District of Columbia. Born in New York City, he received his medical degree from the College of Physicians and Surgeons, Columbia University in 1958. Specialty: Pediatric Ophthalmology.

ADRIAN OLIVER HOSTEN, M.D. Office: Freedmen's Hospital. Born in Grenada, British West Indies, he received his medical degree from Howard University in 1962. Specialty: Internal Medicine.

SUMER CHAND JAIN, M.D. Office: Washington Hospital Center. Born in Delhi, India, he received his medical degree from Agra University in India in 1955. Specialty: Anesthesiology.

MARINO JOSEPH MATURO, M.D. Office: 2412 Minnesota Avenue, S.E. Born in Norwich, Conn., he received his medical degree from the University of Guadalajara, Mexico, in 1964. Specialty: General Practice.

SANDER HOLSTEIN MENDELSON, M.D. Office: Washington Hospital Center. Born in Washington, D. C., he received his medical degree from New York University in 1960. Specialty: Cardiology.

MAHMOUD MOUSAVIPOUR, M.D. Office: Northeast Clinic. Born in Bam, Iran, he received his medical degree from the University of Tehran, Iran, in 1958. Specialty: General Surgery.

JUDITH LIVANT RAPOPORT, M.D. Office: 3246 P Street, N.W. Born in New York City, she received her medical degree from Harvard University in 1959. Specialty: Psychiatry.

RONNIE R. RAY, M.D. Office: 1835 Eye Street, N.W. Born in Louisville, Ky., he received his medical degree from Baylor University in 1960. Specialty: Ophthalmology.

CHARLES ANDREW RIGG, M.D. Office: Children's Hospital of the District of Columbia. Born in Hamilton, Victoria, Australia, he received his medical degree from the University of Sydney in 1950. Specialty: Pediatrics (Adolescent Medicine).

MARVIN B. ROSENBLATT, M.D. Office: 11200 Lockwood Drive, Silver Spring, Md. Born in Chester, Pa., he received his medical degree from Howard University in 1959. Specialty: Obstetrics and Gynecology.

LAURENCE E. RUBIN, M.D. Office: 1302 18th Street, N.W. Born in St. Louis, Mo., he received his medical degree from Washington University in 1960. Specialty: Ophthalmology.

WILLIAM A. SHEVLIN, M.D. Office: Georgetown University Hospital. Born in New York City, he received his medical degree from Georgetown University in 1959. Specialty: Neurosurgery.

## Withdrawal of Drugs—Life-threatening

WITHDRAWAL of barbiturates or other sedative drugs, including the "minor tranquilizers," from persons with strong physical dependance on them may be life-threatening and can only be accomplished satisfactorily in a drug-free environment where hospital and nursing facilities are available.

COMMITTEE ON PROBLEMS OF
DRUG DEPENDENCE
*Washington Psychiatric Society*

N. B. The Committee would appreciate it if members of the D. C. Medical Society will comment on or relate their experiences concerning problems of drug abuse or misuse.

ROBERT ISAAC SIMON, M.D. Office: 1616 18th Street, N.W. Born in Stamford, Conn., he received his medical degree from Tufts University in 1960. Specialty: Psychiatry.

GEORGE ANDREW SOLACK, M.D. Office: 2141 K Street, N.W. Born in Hazleton, Pa., he received his medical degree from George Washington University in 1960. Specialty: Radiology.

CLAUDIUS THOMAS, M.D. Office: 6216 Georgia Avenue, N.W. Born in Grenada, British West Indies, he received his medical degree from Howard University in 1957. Specialty: General Surgery.

LUIGI PETER VECCHIARELLO, M.D. Office: 2412 Minnesota Avenue, S.E. Born in New York City, he received his medical degree from the University of Yucatan, Mexico, in 1963. Specialty: General Practice.

### Associate

DIANA J. EGAN, M.D. Office: 3611 Branch Avenue, Hillcrest Heights, Md. Born in Brooklyn, New York, she received her medical degree from Woman's Medical College of Pennsylvania in 1963. Specialty: Obstetrics and Gynecology.

TIBOR JACK GREENWALT, M.D. Office: American National Red Cross. Born in Budapest, Hungary, he received his medical degree from New York University in 1937. Specialty: Internal Medicine.

GLENN ARTHUR MEYER, M.D. Office: Walter Reed Army Institute of Research. Born in Baraboo, Wisc., he received his medical degree from the University of Wisconsin in 1960. Specialty: Neurological Surgery.

HARVEY WILLIAM RICE, M.D. Office: 8715 First Avenue, Silver Spring, Md. Born in New York City, he received his medical degree from the University of Cincinnati in 1959. Specialty: Child Psychiatry.

### Resident-Intern

JOHN FRANCIS BRESSETTE, M.D Office: Georgetown University Medical Center. Born in Webster, Mass., he received his medical degree from Georgetown University in 1959. Specialty: Urology.

JOHN VINCENT GOLDING, JR., M.D. Office: D. C. General Hospital. Born in New York City, he received his medical degree from Howard University in 1965. Specialty: Radiology.

## Heart Patients Needed at Clinical Center

THE COÖPERATION OF PHYSICIANS is requested in the referral of patients for a study of the most recent advances in treatment of patients with angina pectoris being conducted by the National Heart Institute at the Clinical Center, National Institutes of Health, in Bethesda, Md.

Patients under 60 years of age with severe angina pectoris will be admitted for intensive study to evaluate the severity of the disease and to determine the effectiveness of optimal medical management. Operative intervention will be offered to those patients who are felt to be suitable candidates. Subsequently, follow-up studies will be performed to determine the degree of improvement brought about by these procedures. Upon completion of their studies patients will be returned to the care of the referring physician, who will receive a summary of findings.

Physicians interested in having their patients considered for admission to the Clinical Center for this study may write or telephone Dr. Eugene Braunwald, Clinical Center, Room 7-N-220, National Institutes of Health, Bethesda, Md. 20014; telephone: (301) 656-4000, Ext. 65095.

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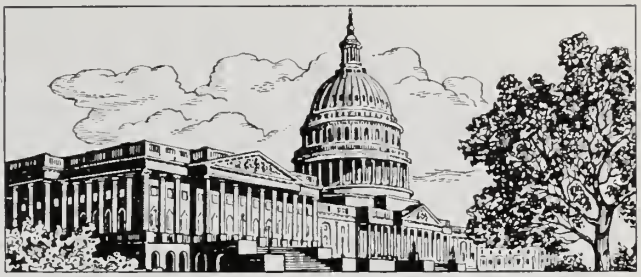

# NEWS & PERSONALS

## Meetings

**A Seminar-Workshop for Physicians** will be held in the building of the Medical Society of the District of Columbia, January 10 and 11, 1968 under the sponsorship of the Medical Society, the D. C. Thoracic Society, and the D. C. Tuberculosis Association. The theme of the Seminar is "The Key Role of the Private Physician in the Diagnosis and Management of Chronic Respiratory Diseases."

Registration will open Wednesday evening at 7:00 p.m. The first session will begin at 8:00 p.m. when Dr. Robert F. Donohoe, President of the D. C. Thoracic Society, will make some opening remarks. Following an introduction of the speakers by Dr. William J. Washington, Dr. Sol Katz, Chief of General Medical Services, Veterans Administration Hospital, will moderate a panel discussion on "Chronic Respiratory Diseases—Definitions, Causes and Manifestations." Panelists will be Dr. Oscar Auerbach, Senior Medical Investigator, Veterans Administration Hospital, East Orange, N.J., and Dr. Thomas Petty, Assistant Professor of Medicine, University of Colorado Medical Center at Denver.

The evening's meeting will close with a social hour and refreshments in the Lounge.

Registration will continue at 12 noon on Thursday, January 11. A "Seminar on Diagnostic Techniques" at 1:00 p.m., in the Exhibit Hall, will be chairmaned by Dr. Donohoe. Subjects to be presented by participating physicians will be:

"Clinical Clues to Diagnosis," Dr. Hall G. Canter, Assistant Chief of Medical Services, Veterans Administration Hospital

"The Role of Spirometry," Dr. Harold M. Silver, Assistant Clinical Professor of Medicine, George Washington University School of Medicine

"The Role of Blood Gases," Dr. Kenneth M. Moser, Chief of the Pulmonary Division, Georgetown University Hospital

Following the seminar time will be allotted for a "Workshop on Diagnostic Equipment" in Rooms A, B and C. On hand to discuss the use of the equipment will be Drs. Canter, Moser, Silver and Dr. Roscoe C. Young, Jr., Director of the Pulmonary Function Laboratory at Freedmen's Hospital.

The scientific session in the Exhibit Hall will resume at 3:00 p.m. with a "Seminar on Therapeutic Techniques." Dr. Maurice A. Sislen, President-elect of the D. C. Thoracic Society, will be chairman. There will be 3 presentations:

"Management of Respiratory Failure," Dr. Robert W. Langevin, Director of the Pulmonary Function Laboratory, Washington Hospital Center

"Management of Infectious Aspects," Dr. James A. Curtin, Chairman, Department of Medicine, Washington Hospital Center

"Long-term Outpatient Management," Dr. James P. Mann, Associate Clinical Professor of Medicine, George Washington University School of Medicine

Following this seminar therapeutic equipment will be on display in Rooms A, B and C, with Drs. Langevin, Mann, and Dr. James D. Shepperd, Clinical Instructor in Medicine, Howard University College of Medicine, available for consultation and discussion.

The meeting will close with a cocktail party in the Lounge beginning at 5:00 p.m.

All physicians are urged to attend. There will be no admission fee. Six hours' postgraduate credit for all G.P. members attending will be granted by the American Academy of General Practice.

## General News

**The Peace Corps** is conducting a nationwide **campaign to recruit staff medical doctors** to meet its growing overseas program. Peace Corps doctors have the responsibility for the health of the volunteers and often participate in local health projects carried out by the volunteers. They receive salaries comparable to those paid in other branches of Government based on experience and qualifications.

It is the first time since the Peace Corps was created in 1961 that the Agency has had to recruit physicians to serve 2 years overseas. A revision of the Selective Service Law by Congress has eliminated draft exemption for Public Health Service doctors serving as Peace Corps physicians.

Peace Corps doctors receive training in Washington in tropical medicine, health education, and programming, in addition to language training. The Agency also provides transportation for the doctor and his family to his overseas assignment plus many other benefits, including storage of possessions left in the United States.

To qualify, physicians must be U.S. citizens, have licenses to practice in any of the 50 states, meet physical requirements, and must never have served in any capacity with an intelligence agency of the Government.

Interested physicians should contact Dr. Stanley C. Scheyer, Director of the Agency's medical programs, at 806 Connecticut Avenue, N.W., Washington, D. C. 20525; telephone (202) 382-2308.

At its dinner meeting, October 20, the **D. C. Allergy Society** elected officers for 1967-68. They are:

Dr. Solomon E. Barr, *President-elect*; Dr. Robert T. Scanlon, *Secretary-Treasurer*; and Drs. Halla Brown and Gilbert D. Barkin, *members of the Executive Committee.*

Dr. Roland B. Scott took office as President of the Society.

**The Washington, D. C. Dermatological Society** has new officers. They are:

Lt. Colonel Louis E. Harman, *President*; Dr. Harold J. Berman, *Vice President*; and Dr. John A. Kenney, Jr., *Secretary-Treasurer.*

**Georgetown University School of Medicine** has been awarded $50,000 by the Avalon Foundation for scholarships to be granted medical students "on a combined basis of financial need and scholastic attainment." Scholarships provided under the grant will be known as the Avalon Foundation Scholarships. Eleven private medical schools participated in Avalon's million-dollar scholarship grant.

# Personals

**Dr. Sidney L. Werkman** became the Deputy Director of the Joint Commission on Mental Health of Children in September. The Commission, based in Washington, D. C., was created by an Act of Congress and has the responsibility of assessing the present and future resources and needs in the field of emotional disorders and mental health of children and adolescents; it will report to the Congress and to the Nation on its findings. Dr. Werkman is Director of the Division of Adolescent Psychiatry at Children's Hospital of D. C. and Associate Clinical Professor of Psychiatry at George Washington University School of Medicine.

**Dr. Clifton R. Brooks** was Chairman of a Flight Training Course for doctors during the Annual Meeting of the Flying Physicians Association at Williamsburg, Va., September 10-15. This was its first course to train doctors in flying seaplanes. Fifteen physicians and 2 wives took the course and received seaplane ratings from the Federal Aviation Administration. At the same meeting Dr. Brooks presented a paper on "The Role of Allergies in Flight Fitness" with special reference to cigarette smoking and passenger comfort.

**Dr. Robert S. Poole** took first place in the golf tournament which was held in conjunction with the Association's scientific meeting.

**Dr. William G. Battaile,** who is head of pathology at Sibley Memorial Hospital and associated with the Hunter Memorial Laboratories, was elected Secretary of the American Association of Blood Banks at its Annual Meeting in New York in October.

**Dr. James E. Fitzgerald** has been appointed Volunteer Disaster Medical Consultant to the American Red Cross, in which capacity he will serve as adviser to the national director of Disaster Service in the establishment of working relationships with physicians, hospitals, and public health agencies. Dr. Fitzgerald is Clinical Associate Professor of Medicine at Georgetown University School of Medicine.

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**FREE VISION SCREENING TESTS were given to over 500 4- and 5-year-old children by the Prevention of Blindness Society of Metropolitan Washington (UGF) on October 1, 2, and 3, at the D. C. Medical Society Building. Approximately 50 of the children did not pass the vision test and were referred for medical eye examination; 13 were referred because of possible muscle imbalance. These free tests were a joint community service of the D. C. Medical Society and the Prevention of Blindness Society in order to find possible eye defects early when corrective treatment is most effective. Posing for this picture was a representative group of youngsters from Preschool Play Centers brought in by buses supplied by the D. C. Recreation Department. On Sunday working mothers were able to accompany their own children.**

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# Correspondence

To the Assistant Editor:

The September issue of the Medical Annals of the District of Columbia dedicated to Dr. Wallace M. Yater was a most appropriate tribute. Dr. Mattingly detailed Dr. Yater's medical achievements, his contributions as a teacher, investigator, clinician, and the impact he had on Dr. Mattingly's career. Dr. Ecker, as President, cited the Society's indebtedness to this great physician.

Dr. Yater's life influenced many physicians beyond the areas mentioned. As a member of the Society, representing other physicians affected by his example, I wish to add this personal note as a tribute to Dr. Wallace Yater. Although words are inadequate to express one's indebtedness to Dr. Yater, nevertheless the effort is ennobling. Dr. Yater's presence set the tone and elevated the level of the practice of medicine in Washington, D. C. He was an inspiration to all young internists who joined the Medical Society and personifies, what is so difficult to define, the True Internist. He is an unparalleled diagnostician who combines the Science and Art of Medicine in exquisite proportions.

It is regrettable that the present generation of doctors have been denied the privilege of attending his Grand Rounds at D. C. General Hospital (formerly Gallinger Hospital). There, students, house staff, and physicians in private practice gleaned "pearls of wisdom" from him and his associates, notably Drs. Hugh H. Hussey and Sol Katz. The Rounds were always clinical, concerned with the immediate problem at hand, and provided a forum to elaborate on current concepts of pathophysiology and therapy. The physician observed the skill in extracting pertinent and new facts from the history, subtle physical signs that escaped the inexperienced, and the use of laboratory tests in the differential diagnosis. Treatment was pertinent to the problem and generalities rarely offered. Different viewpoints were accepted if stoutly supported by fact and not mere opinion. Rounds were a rewarding, sometimes chastening, but never easily forgotten experience.

Perhaps the greatest tribute to Dr. Yater is to be found among the countless physicians whose lives he has touched and inspired to emulate him in their daily practice of Internal Medicine.

Dr. Yater remains a Doctor's Doctor! He is truly the Compleat Physician.

Benjamin Manchester, M.D.

To the Editorial Board:

### A Salute to a Distinguished Medical Editor

It is with a great deal of pleasure that I write these lines about one of the country's outstanding physicians with whom it was my privilege to be associated for many years. Dr. Wallace Mason Yater is not only well known to all of his colleagues in the District of Columbia but to physicians in his field nationally. It was in Washington that he became a medical educator of first rank and a highly successful and respected practicing physician.

Despite the honors and recognition which have come his way he has had a special interest in the Medical Annals of the District of Columbia, of which he has been the Editor for the past 35 years.

There is something about being responsible for a publication that becomes a part of one. As I wrote in the Medical Annals in 1951, on the occasion of Dr. Yater's 20 years as Editor: "Dr. Yater has considerable talent and liking for his avocation, otherwise he would long since have thrown in the sponge. Editing and writing are in his blood. He, like his colleagues in this field, finds genuine pleasure in creative effort." The

Medical Annals under his guidance has become one of the leading state medical journals in the country.

Despite Dr. Yater's satisfaction with the success of the Medical Annals, deadlines must be met and they can become very burdensome. Each scientific article must be carefully read and edited. Articles of a general nature must also be scrutinized, for the Editor is responsible for everything that appears in the publication. Drudgery, yes—but as I have pointed out, there are compensations which make it all worthwhile.

I wish to join with the many appreciative readers of the Medical Annals in saluting Dr. Yater for his years of devotion to the Medical Society's publication and for the high standard it has attained under his direction.

Theodore Wiprud

# Obituaries

## Francis Thomas Coleman, Ph.B., M.D.

(1909–1967)

Dr. Francis T. Coleman, Director of Student Medical Services at Catholic University for 13 years, died, October 15, 1967 at his home, 5315 16th Street, N.W.

Dr. Coleman was born in Providence, R.I., March 9, 1909. He received his baccalaureate degree from Providence College in 1930, then came to Washington to attend Georgetown University School of Medicine, graduating in 1934. He interned at St. Joseph's Hospital in Baltimore the following year and served a 2-year residency in general surgery at the same hospital. From 1937 to 1939 he was Assistant Chief Surgeon at Northern Maine General Hospital in Aroostook County.

Dr. Coleman began his practice in the District of Columbia in 1939, serving on the surgical staffs of Georgetown University and Sibley Memorial Hospitals. For several years he was on the faculty of Georgetown University as Clinical Instructor in Surgery. In addition to being University doctor at Catholic University, he was head of the infirmary and team physician. He maintained offices at his home.

During World War II Dr. Coleman trained as a flight surgeon and served with the U. S. Air Corps in England. He was on active duty for more than 3 years and was discharged with the rank of Major.

He was an Active member of the Medical Society of the District of Columbia from 1940, a member of the American Medical Association, the Aerospace Medical Association, and the American College Health Association.

He leaves his wife, Mrs. Helen Hile Coleman, and 3 sons, Joseph M., and Jerome P., of the home address, and Francis T., Jr., of Sumner, Md. He also leaves a brother, Ambrose A., of Providence, R.I., and a sister, Mrs. Helen Hayden, of Washington.

## Charles Perry Howze, B.S., M.D., F.A.C.S

(1895–1967)

Dr. Charles P. Howze, who specialized in the practice of urology in Washington for many years, died in Charlottesville, Va., October 26, 1967.

Dr. Howze was born in Marion, Alabama, on February 7, 1895. He received his Bachelor of Science degree from Marion Institute of Marion, Alabama, in 1914 and his medical degree from the University of Virginia at Charlottesville in 1918. He interned in surgery at the New York Post-Graduate Hospital for 2 years, 1918 to 1920, and trained in urology at the Brady Urological Institute of Johns Hopkins in 1922 and at the University of Virginia Hospital from 1922 to 1925.

Dr. Howze was licensed in the District of Columbia in 1929. He served on the faculty of George Washington University School of Medicine as Associate in Urology from 1932 to 1945. He was on the hospital staffs of Garfield, Emergency, Children's, Episcopal Eye, Ear and Throat, and consultant in urology to Mt. Alto Veterans Hospital before he moved to Charlottesville in 1953.

Dr. Howze was a diplomate of the American Board of Urology, a Fellow of the American College of Surgeons, and a member of the American Medical Association, the Southern Medical Association, the Medical Society of Virginia, the Southern Surgical Association, the American Urological Association, and many other surgical and urological societies. He was an Active member of the Medical Society of the District of Columbia from 1930 until he resigned in 1953.

His wife, Mrs. Hanna Howze, of 919 Rugby Road, Charlottesville, survives him, together with 2 sons, John Howze, of Alexandria, Va., and Charles P. Howze, Jr., of Washington.

## Martin Barbour Hiden, M.D.

(1886–1967)

Dr. Martin B. Hiden, retired surgeon of Warrenton, Va., died, September 21, 1967, in the Fauquier Hospital in Warrenton which he founded. The Hospital was formerly known as the Physicians Hospital.

Dr. Hiden was born in Fork Union, Va., June

6, 1886. He graduated from the University of Virginia School of Medicine in 1911. He interned at the Retreat for the Sick in Richmond for a year and was resident physician at the Washington Asylum Hospital, in Washington, D. C. for a year.

He served in the Regular Medical Corps of the U. S. Navy from 1914 to 1921 and last held the rank of Lt. Commander. He did postgraduate work at Rockefeller Institute, at the Mayo Clinic, and at Tulane Medical School.

After leaving the Navy in 1921 Dr. Hiden began his private practice in Warrenton. A general surgeon, he was associated with the Loudoun County Hospital in Leesburg, the Alexandria (Va.) Hospital, and Doctors Hospital in Washington.

Dr. Hiden purchased a building in Warrenton in 1941 and the following year opened the Physicians Hospital. He was Chairman of the Board of Directors of the Hospital and continued his practice there until he retired in 1954. Fauquier County then purchased the hospital and renamed it Fauquier Hospital.

Dr. Hiden was a member of the American Medical Association, the Southern Medical Association, and a member and Past President of the Loudoun County Medical Society and the Fauquier County Medical Society. He had served as Vice President of the Medical Society of Virginia. He was elected to Associate membership in the Medical Society of the District of Columbia in 1939 and retained his membership until 1958.

He leaves a daughter, Mrs. John A. Gibson, Jr., of Triangle, Va.

## Harold Willard Glattly, B.S., M.D.

(1902–1967)

Dr. Harold W. Glattly, a staff member with the Division of Medical Sciences of the National Academy of Sciences-National Research Council, died, October 26, 1967 at Walter Reed General Hospital. Dr. Glattly had been an officer in the United States Army and retired with the rank of Brigadier General in February 1957.

Born in Mora, Minnesota, September 15, 1902, Dr. Glattly received his Bachelor of Science degree from the State University of Iowa in 1924 and his medical degree from the same University in 1926. Entering military service at graduation, he interned at Letterman General Hospital in San Francisco. During his long Army career he received numerous decorations in recognition of distinguished service.

Following his retirement from the Army, Dr. Glattly became associated with the National Research Council, where he served as Executive Secretary of 3 committees in the Division of Medical Sciences, namely, the Committees on Prosthetic-Orthotic Education, Skeletal System, and Genital-Urinary System.

He was elected to Associate membership in the Medical Society of the District of Columbia in 1965. He had been a member of the American Medical Association until recently and was a member of the American Congress of Physical Medicine and Rehabilitation. He was Secretary of the National Medical Veterans Society.

His wife, Mrs. Sally Ann Wier Glattly, died recently. He leaves a daughter, Jan, of the home address, 3909 Calverton Drive, Hyattsville, Md., and 2 sons, William R., of Washington, and Charles, of Reno, Nevada.

## Robert Joseph Barrett, M.D.

(1917–1967)

Dr. Robert J. Barrett, an Associate member of the D. C. Medical Society, died, October 2, 1967, at Suburban Hospital in Bethesda, Md., where he was Chief Otolaryngologist. He had practiced in suburban Washington since 1948.

Dr. Barrett was a native Washingtonian, born, September 22, 1917 to Robert J. and Theresa C. Barrett. He studied premedicine at Georgetown University from 1935 to 1938 and graduated in medicine from Georgetown in 1942. He interned at Providence Hospital for a year.

Following his internship Dr. Barrett enlisted in the Army Medical Corps and was commissioned Captain; he served in the European theater during World War II with the 93rd Medical Battalion. After the war he continued his training as resident physician at the Episcopal Eye, Ear and Throat Hospital for 2 years, 1946–48.

He was Clinical Instructor in Otolaryngology at Georgetown University School of Medicine from 1948 to 1957. In addition to Suburban he was affiliated with Holy Cross, Children's, Georgetown, and Providence Hospitals, and the Washington Hospital Center.

Dr. Barrett was elected to Associate membership in the Medical Society of the District of Columbia in 1951. He was a member of the Montgomery County (Maryland) Medical Society.

He leaves his wife, Mrs. Agnes McGann Barrett, of their home, 12016 Claridge Road, Silver Spring, Md.

# MEDICAL ANNALS OF THE DISTRICT OF COLUMBIA

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- Ahnfeldt, A. L., editor-in-chief; Allen, K. D. A., editor for radiology; McFetridge, E. M., and Stein, M. W., associate editors: Medical Department, United States Army: Radiology in World War II, (Bickham) Adv. (July) 35
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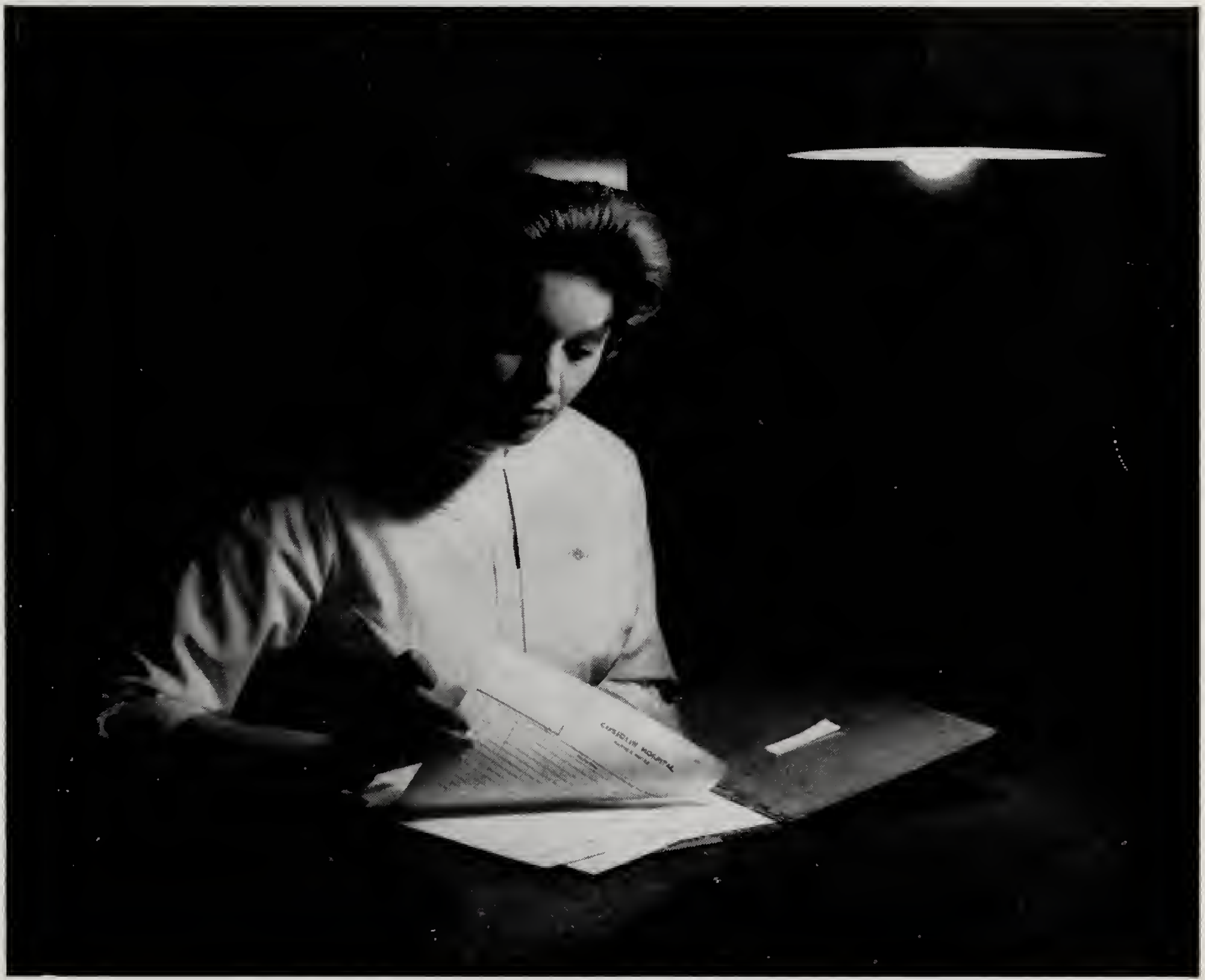

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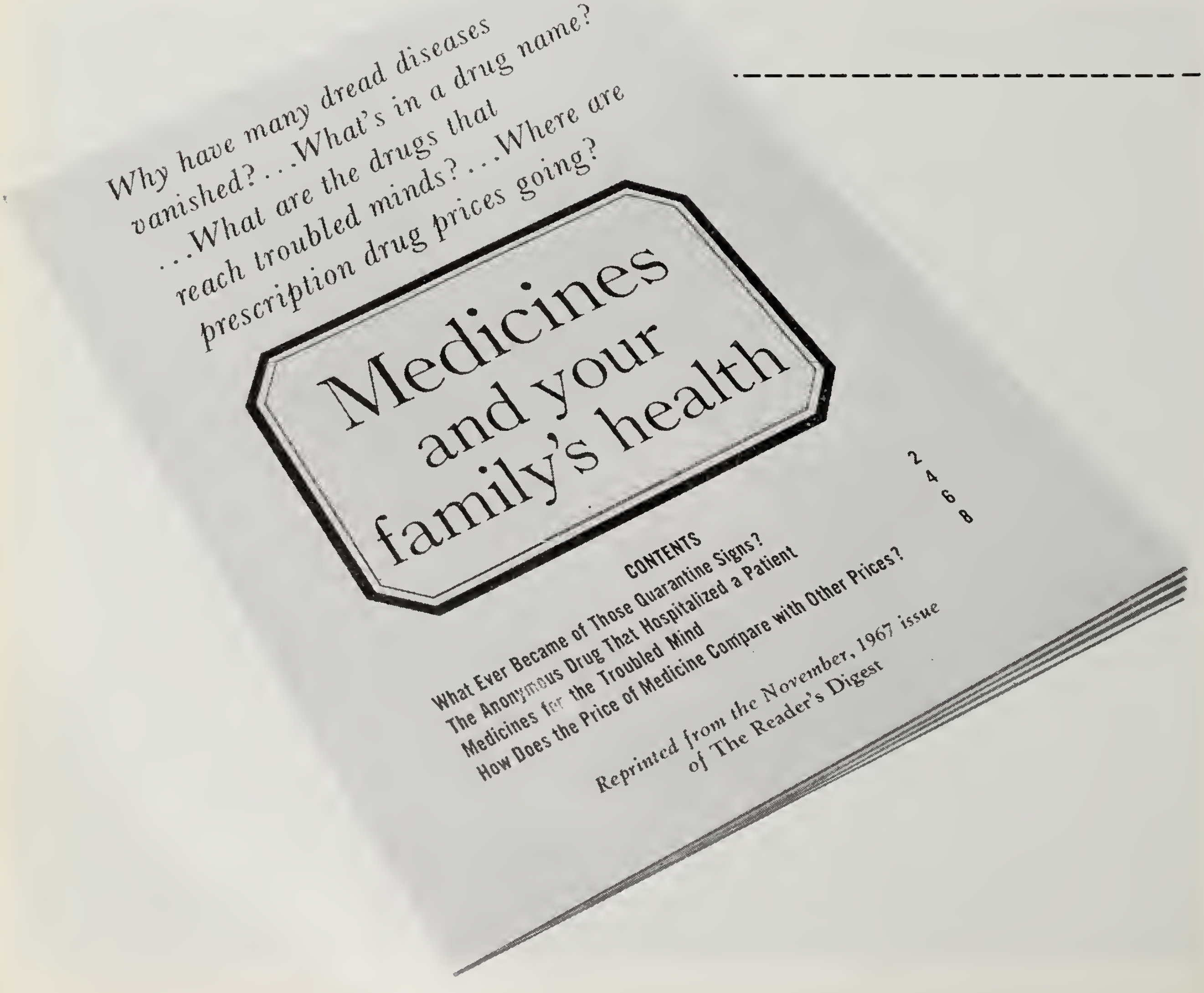

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# NEW PAMPHLETS

Many publications containing timely information for physicians as well as informative literature for their patients are coming into the Executive Offices of the Medical Society in increasing numbers. Following are some of those recently received or mentioned in news releases:

### AMA Publications

(Available from the Order Department, American Medical Association, 535 North Dearborn Street, Chicago, Ill. 60610.)

**Continuing Professional Education Programs of Voluntary Health Agencies.** Presents major purpose and type of continuing professional education programs offered by 10 major National Voluntary Health Agencies. 28 pp.

**The Crutch That Cripples: Drug Dependence.** Committee on Alcoholism and Drug Dependence, Council on Mental Health, American Medical Association. Designed for the public. 25 pp. Price, 25 cents.

**Group Practice: Guidelines to Forming or Joining a Medical Group,** 2nd rev. American Association of Medical Clinics, American Medical Association, and Medical Group Management Association. 40 pp.

**Manual on Alcoholism.** For use by physicians, the manual contains a description of the metabolism and pharmacology of alcohol, and offers suggestions on diagnosis and the physical, psychological, and sociological aspects of treatment. 87 pp. Price, 50 cents.

**The Physician's Career.** A teaching outline on medical practice and community relations for physicians and medical students. 99 pp. Price, 75 cents.

### HEW Publications

(Available from the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C. 20402. Single copies of most of these are available free upon request from the Public Health Service, Washington, D. C. 20201.)

**Coronary Care Units. Specialized Intensive Care Units for Acute Myocardial Infarction Patients** (PHS Publ. No. 1250). 40 pp. Price, 20 cents.

**Cystic Fibrosis** (PHS Publ. No. 1077). National Institute of Arthritis and Metabolic Diseases. Written in nontechnical language, the leaflet presents authoritative, up-to-date background information on cystic fibrosis. Price, 5 cents.

**Lead Poisoning in Children** (Children's Bureau Publ. No. 452–1967). Jane S. Lin-Fu, M.D. Designed for all health workers, it is a guide in planning an effective approach to the prevention of this health problem. 25 pp. Price, 15 cents.

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**National Institute of Mental Health Support Programs** (PHS Publ. No. 1700). A comprehensive guide to Federal support of mental health research, training, and community services. 54 pp.

**Treating Cancer** (PHS Publ. No. 690). National Cancer Institute. Issued for the general public, it describes current methods of treating cancer by surgery, radiotherapy and chemotherapy. 20 pp. Price, 20 cents.

### Miscellaneous

**Immunization for All** (Public Affairs Pamphlet No. 408). Jules Saltman. How the human body resists infection and an outline of the immunizations available. 28 pp. Price, 25 cents. Public Affairs Committee, 381 Park Avenue South, New York, N.Y. 10016.

**A National Directory of Clinic Facilities for the Diagnosis and Treatment of Epilepsy** (listed by states). 68 pp. The Epilepsy Foundation, 1419 H Street, N.W., Washington, D. C. 20005.

**What Is An Otolaryngologist?** Prepared as a public service by the American Academy of Facial Plastic and Reconstructive Surgery, Inc. Price (4-page leaflet), $2.50 per 100. Jack R. Anderson, M.D., 1111 Tulane Avenue, New Orleans, La. 70112.

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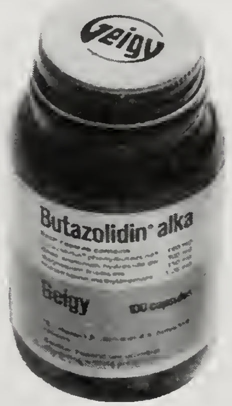

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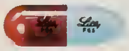

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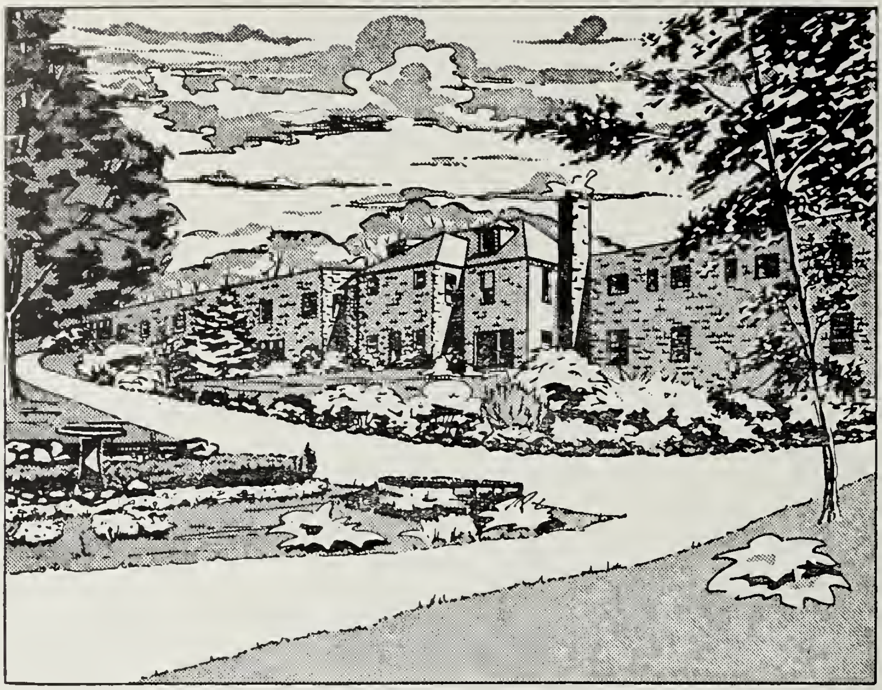

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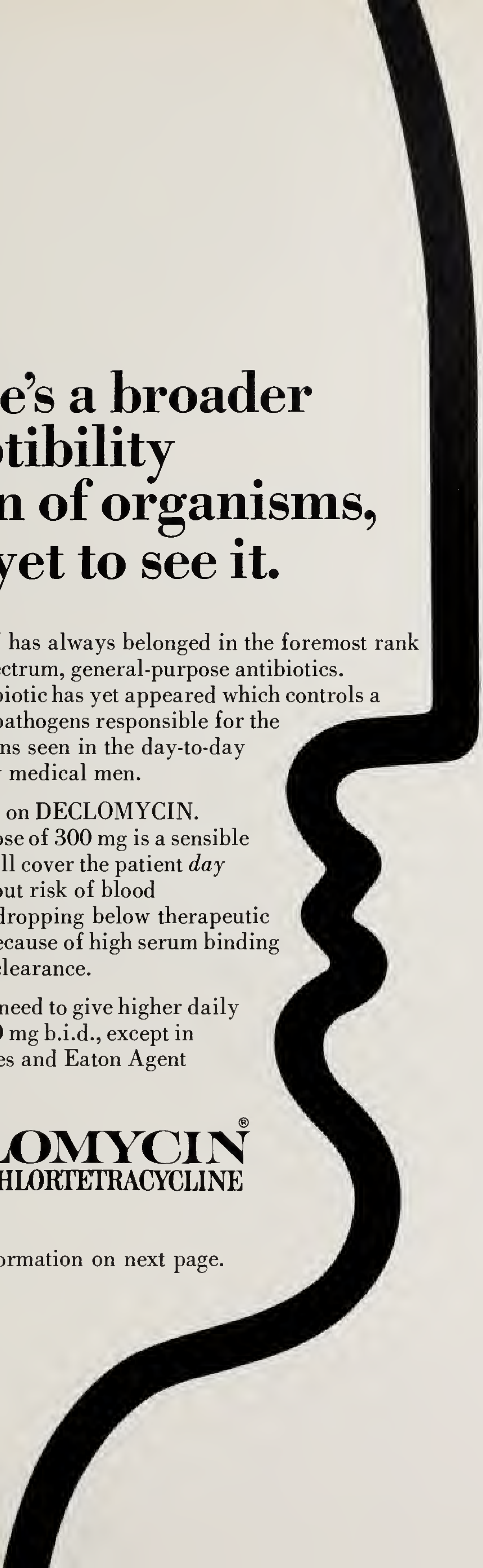

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**Warning**—In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, lower than usual doses are indicated, and, if therapy is prolonged, serum level determinations may be advisable. A photodynamic reaction to natural or artificial sunlight has been observed. Small amounts of drug and short exposure may produce an exaggerated sunburn reaction which may range from erythema to severe skin manifestations. In a smaller proportion, photoallergic reactions have been reported. Patients should avoid direct exposure to sunlight and discontinue drug at the first evidence of skin discomfort. Necessary subsequent courses of treatment with tetracyclines should be carefully observed.

**Precautions**—Overgrowth of nonsusceptible organisms may occure. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

**Side Effects**—Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes. A rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose related. Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth— dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs discontinue medication and institute appropriate therapy.

**Average Adult Daily Dosage:** 150 mg q.i.d. or 300 mg b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

In the treatment of syphilis a dosage schedule of a total of 12 to 18 Gm. given in equally divided doses over a period of 10 to 15 days should be followed. Close follow-up observation of the patient is recommended, including appropriate laboratory tests, since demethylchlortetracycline has not had adequate evaluation in all stages of syphilis. Spinal fluid examination should be included as part of this follow-up.

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*Classified advertisements of a professional nature are free to members.*

## SITUATIONS WANTED

INTERNIST with clinical hematology and cancer chemotherapy training, presently at Johns Hopkins, Board-eligible, AOA, aged 32, married, military service completed, desires association with internist or group in Washington, D. C. area. Available June 1968. For interview address Allen M. Mondzac, M.D., 2225 Rogene Drive, Apt. 201, Baltimore, Md. 21209; or telephone 764-0870.

GENERAL SURGEON, Board-eligible, Virginia licensed, desires part-time partnership or to share office in Northern Virginia. Telephone Dr. Trinidad, 541-1000; evenings, 656-3708.

INTERNIST, 32, Board-eligible, with hematology and oncology subspecialty training, military fulfilled, seeks association leading to partnership with other internists in Washington, D. C. area. Address: Box 12, 2007 Eye Street, N.W., Washington, D. C. 20006.

PATHOLOGIST, Board-eligible, AP, CP, January 1, 1968. Licensed in D. C. and Virginia. Desires position leading to full partnership. Address Box 1, 2007 Eye Street, N.W., Washington, D. C. 20006.

PHYSICIAN, 45, tired of 9 to 7-plus practice, seeking salaried position with regular hours, e.g., position involving travel and administrative work. Board-qualified in internal medicine, pulmonary disease, allergy; presently engaged in busy practice with particular emphasis on allergy. Telephone 929–1085 after 7:30 p.m. and 935–0013 during day.

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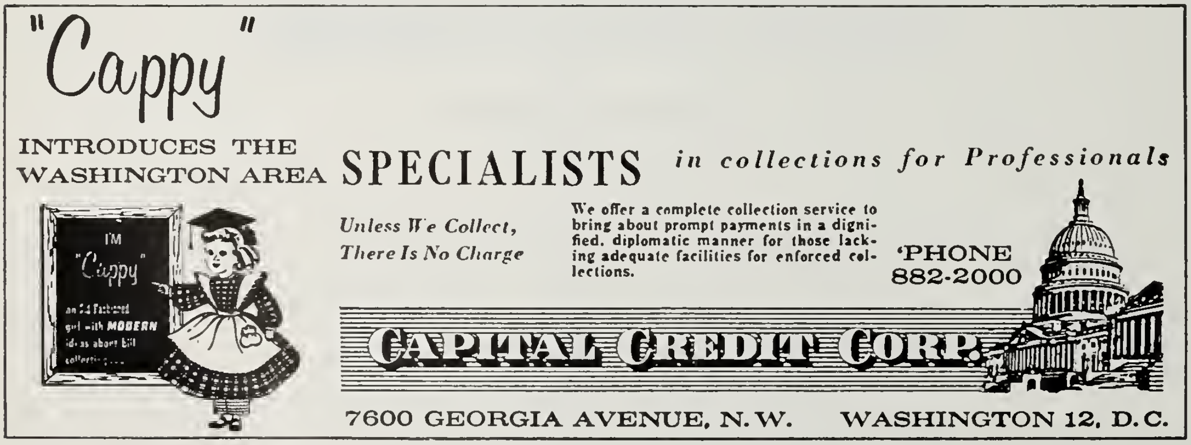

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# BOOKS RECEIVED

Acknowledgment is made of the following books which have recently been received.

**Symposium on Glaucoma. Transactions of the New Orleans Academy of Ophthalmology.** M. F. Armaly, M.D., B. Becker, M.D., J. S. Haas, M.D., P. C. Kronfeld, M.D., I. P. Pollack, M.D., R. N. Shaffer, M.D., and L. E. Zimmerman, M.D. Price, $17.50. Pp. 306, with 120 figures. St. Louis: Mosby, 1967

**Synopsis of Gynecology,** 7th ed. Daniel Winston Beacham, M.D., and Woodard Davis Beacham, M.D. Price, $8.50. Pp. 384, with 105 figures and 1 color plate. St. Louis: Mosby, 1967.

**Diagnostic Procedures in Gastroenterology. With Nurse's Notes and Supplements on Instructions to Patients and Dietary Treatment.** Edited by Charles H. Brown, M.D., with 21 contributors. Price, $19.75. Pp. 438, with 105 figures and 4 color plates. St. Louis: Mosby, 1967.

**Patterns of Living and Housing of Middle-aged and Older People.** Proceedings of Research Conference on Patterns of Living and Housing of Middle-aged and Older People, March 21–24, 1965, Washington, D. C. PHS Publ. No. 1496. Frances M. Carp, Scientific Editor, and Wanda M. Burnett, Technical Editor. Price (paper), $1.00. Pp. 181, illustrated. Washington, D. C. 20402: U.S. Government Printing Office, 1967.

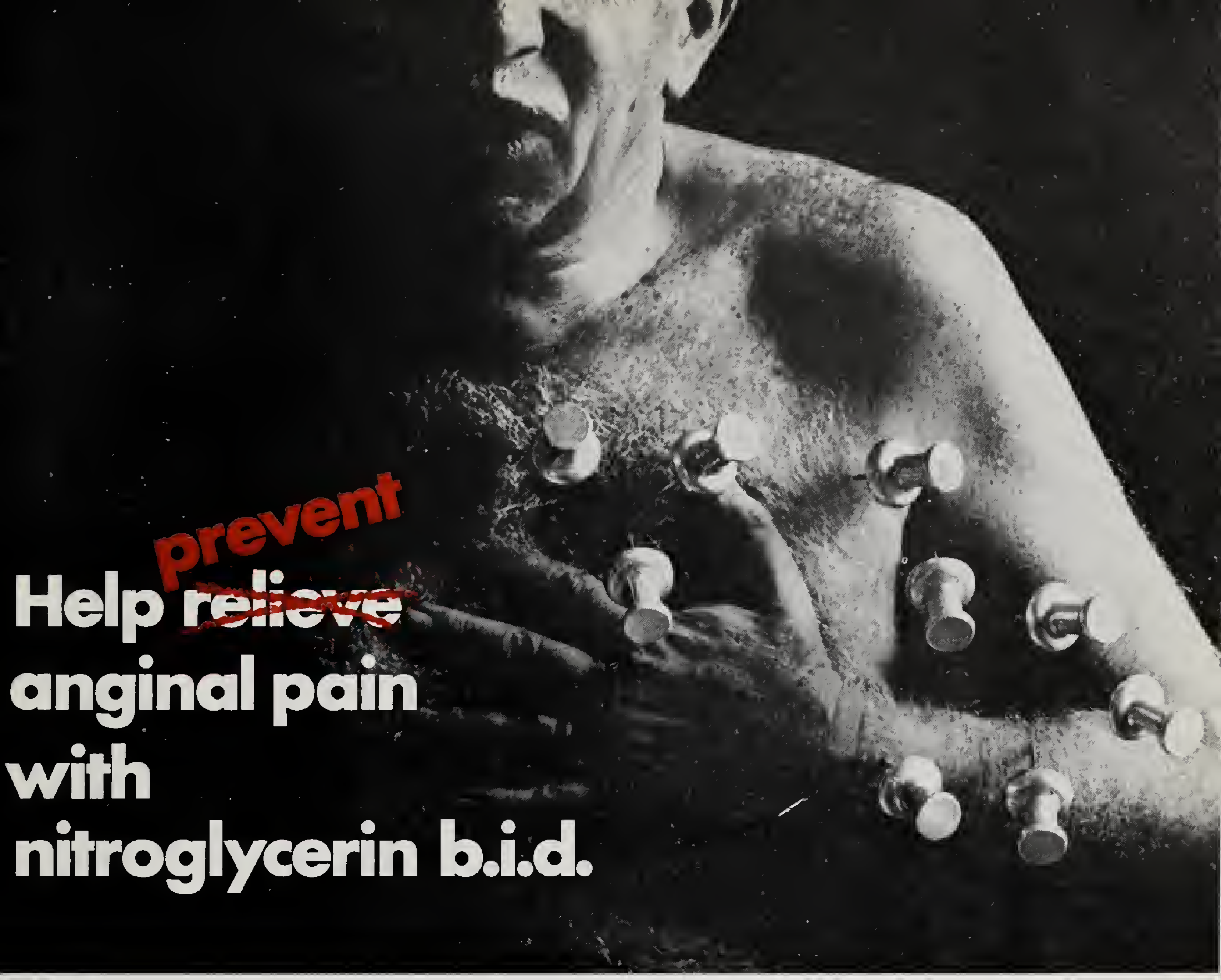
**Diabetes Mellitus: Diagnosis and Treatment.** Volume II. Prepared under the auspices of the Committee on Professional Education of the American Diabetes Association, Inc. George J. Hamwi, M.D., and T. S. Danowski, M.D., Editors. Price, $2.50. Pp. 250. New York: American Diabetes Association, 1967.

**Myotatic, Kinesthetic and Vestibular Mechanisms. Ciba Foundation Symposium.** Edited by A. V. S. deReuck and Julie Knight. Price, $13.50. Pp. 331, with 169 illustrations. Boston: Little, Brown, 1967.

**Medicare and the Hospitals: Issues and Prospects. Studies in Social Economics.** Herman M. Somers and Anne R. Somers. Price, $6.75 (paper, $2.50). Pp. 303. Washington, D. C.: The Brookings Institution, 1967.

**Roentgenologic Diagnosis. A Complement in Radiology to the Beeson and McDermott Textbook of Medicine,** Volumes I and II. J. George Teplick, M.D., Marvin E. Haskin, M.D., F.A.C.P., and Arnd P. Schimert, M.D. Price, $38.00 per set. Pp. 1198, illustrated. Philadelphia: Saunders, 1967.

**Ciba Foundation Study Group No. 29. Antilymphocytic Serum.** Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Maeve O'Connor, B.A. Price, $4.25. Pp. 165, with 37 illustrations. Boston: Little, Brown, 1967.



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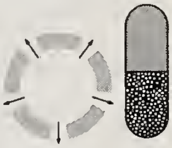

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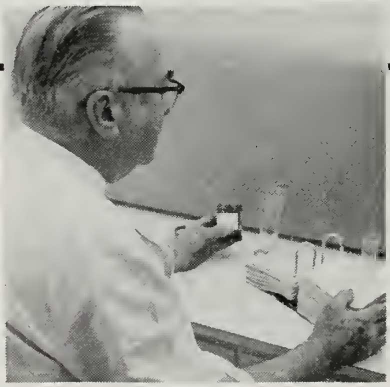

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**Warning:** Not of value in the treatment of psychotic patients, and should not be employed in lieu of appropriate treatment.

**Precautions:** Limit dosage to smallest effective amount in elderly or debilitated patients (not more than 1 mg, one or two times daily initially) to preclude ataxia or oversedation, increasing gradually as needed or tolerated. As is true of all CNS-acting drugs, until correct maintenance dosage is established, advise patients against possibly hazardous procedures requiring complete mental alertness or physical coordination. Driving during therapy not recommended. In general, concurrent use with other psychotropic agents is not recommended. If such combination therapy is used, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium (diazepam), such as phenothiazines, barbiturates, MAO inhibitors and other antidepressants. Advise patients against simultaneous ingestion of alcohol or other CNS depressants. Safe use in pregnancy not established. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Observe usual precautions in impaired renal or hepatic function. Periodic blood counts and liver function tests advisable in long-term use. Cease therapy gradually.

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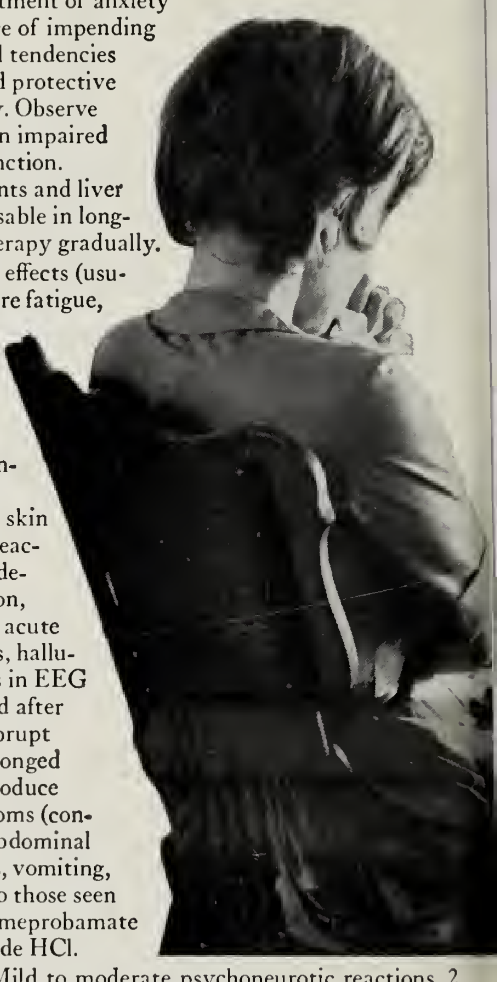

**Dosage:** *Adults:* Mild to moderate psychoneurotic reactions, 2 to 5 mg b.i.d. or t.i.d.; severe psychoneurotic reactions, 5 to 10 mg t.i.d. or q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; muscle spasm with cerebral palsy or athetosis, 2 to 10 mg t.i.d. or q.i.d. *Geriatric patients:* 1 or 2 mg/day initially, increase gradually as needed and tolerated. (See Precautions.)

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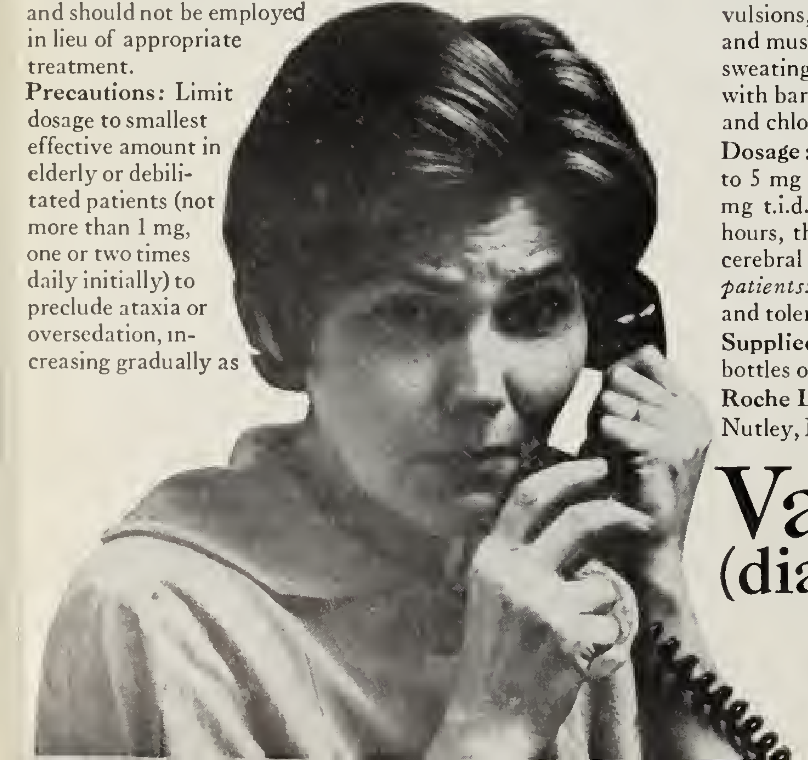

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